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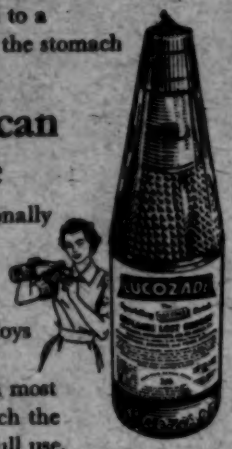

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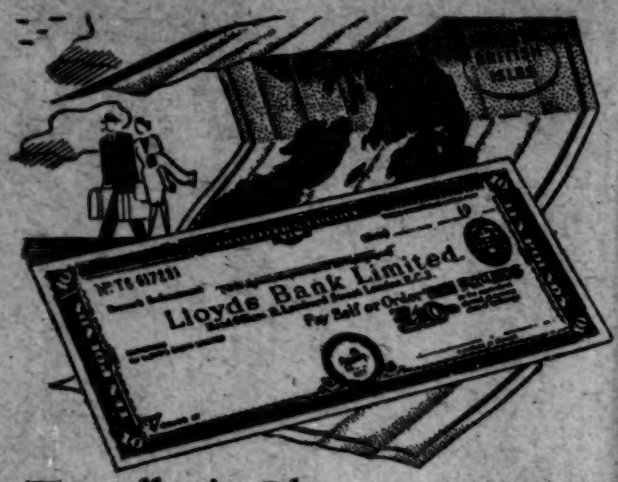

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY NOVEMBER 27 1954

HYPERTENSION AND ITS CONTROL BY HEXAMETHONIUM

BY

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High blood pressure, with its cardiovascular and renal consequences, is perhaps the greatest barrier to survival after middle-age. As in other chronic progressive and so far incurable maladies, the multiplicity of vaunted remedies serves only to emphasize their failure to bring lasting benefit. In fact, for milder degrees of essential hypertension no medicament or specific treatment has yet been shown to rival the benefit produced by adjustments of regime, diet, habits, and weight. For the more severe grades of essential hypertension the past decade has brought methods of attacking the neural mechanisms which, though they may not cause hypertension, are part of the means by which it is maintained. These forms of treatment are surgical (lumbo-dorsal sympathectomy) and medical (by various ganglion-blocking substances, notably hexamethonium compounds). For a treatment of hypertension to be acceptable it must be available for use by general practitioners for patients living at home and pursuing their daily work ; no treatment that depends upon continuous intricate control in a clinic or through an institution is of real value in a disease which is so common and widespread and which often covers one or two or more decades of a patient's life.

In this paper we report the treatment and follow-up of 83 patients who have received hexamethonium bromide for hypertension. The criteria upon which the results of such treatment must be based are discussed, a special distinction being drawn between lowering of blood pressure and prolonging life. The indications and methods for the use of hexamethonium, and the significance and control of side-effects, are considered. Finally, recommendations are made concerning the safeguards needed for induction of this treatment and the manner in which it may be maintained at home and in work.

Ever since a raised blood pressure became recognized as a frequent primary anomaly and was named essential hypertension it has been presumed that the pressure should be reduced if possible. It was recognized that removal of the cause would be the ideal aim, but as the cause remained unknown lowering of the blood pressure would be the means of delaying the many disasters of which hypertension seemed to be the immediate precursor. In those days there was no sure means of diminishing a high blood pressure, although rest in bed and sedatives would help. Sometimes pressure fell spontaneously (owing usually to heart failure or to cardiac infarction), and it was noticed in these cases that the patient's condition at the same time deteriorated. By analogy, it was sometimes explained to hypertensive individuals that even if their pressure could be lowered they would not feel any better for it, the implication being that if the pressure was raised it was a compensation of some sort that was inevitable and necessary, although harmful in the long run.

Teleological and often contradictory notions such as these were but examples of the many arguments prevailing up to the time of the second world war. Now that there are means of lowering high blood pressure in a fairly controlled manner the opportunity arises to test many of these unfounded assumptions. Over several decades writers on the treatment of hypertension have agreed upon certain basic requirements, mainly the need for readjusting the patient's mode of life and the advisability of moderation in diet. Also they have all suspected that the intake of salt should be restricted. Although it has only comparatively recently been decided which element of sodium chloride is the undesirable one, the restriction of salt (and sodium in any combination) remains to-day an integral and important part of treatment.

The effects of any new form of treatment have always had to bear comparison with the well-known results of "conservative" measures comprising essentially avoidance of physical and mental stress, an increase in the hours of rest, the use of sedatives, the reduction of obesity if it existed, and the moral support of a medical attendant. This is still the treatment adopted by physicians when the newer medicinal, dietetic, and surgical measures have been judged inadvisable or ineffective. It is capable of bringing substantial subjective improvement and some reduction in the pressure in about two-thirds of those who conscientiously follow such a regime.

The advantageous effects of a diet consisting only of rice have been described by Kempner (1949). Such a diet, which is very low in protein and contains less than 0.5 g. of sodium in the 24 hours, is capable of lowering the blood pressure and bringing other objective benefits such as improvement in the state of the retinae and

regression of the electrocardiogram towards a more normal form. In general, patients have not been able to tolerate this monotonous diet for long periods, and it has been found that a more liberal diet, provided it contains less than 0.5 g. of sodium daily, may give results nearly as good. Emphasis is placed upon this prevailing notion, which later became a proved fact, that salt was in some way linked with the existence of essential hypertension, as it is an important part of the hexamethonium treatment.

About the time that the results of Kempner were being made known Smithwick (1948) published his results of dorso-lumbar sympathectomy for hypertension. Hailed at the time as a fairly sure and reasonably safe method of bringing down the blood pressure, it was widely practised until, with the passage of years, it became clear that even with the most extensive sections of the sympathetic a lasting reduction of pressure was conferred on only a minority of patients (Evelyn *et al.*, 1949). This did not necessarily mean that the tenure of life was not on the whole increased, and it is believed by those who used the surgical method in properly selected patients that it has often materially improved the prognosis (Hammarström and Bechgaard, 1950; Smithwick, 1951; Morrissey *et al.*, 1953).

Ganglion-blocking Agents

Soon after the popularity of sympathectomy was reaching its height came the first observations on ganglion-blocking agents. Arnold and Rosenheim (1949) employed pentamethonium iodide intravenously and intramuscularly, and found that it produced transient lowering of pressure in hypertensive patients and sometimes even excessive reduction needing correction by adrenaline injection. In the following year were published the papers of Restall and Smirk (1950) and Turner (1950) on the use of hexamethonium bromide. There followed the series of Smirk and Alstad (1951) based on the treatment of 53 patients. These writers selected for treatment the more severe grade of hypertension, including patients showing papilloedema and other vascular retinopathies, cardiac asthma, hypertensive heart failure, and encephalopathy; they concluded that, apart from some of the cases with impairment of renal function, almost all hypertensives can have their blood pressure controlled by these drugs. McMichael (1952) has given qualified approval of parenteral hexamethonium treatment based on a series of 27 cases, and more recently Moyer *et al.* (1953) have, among 58 patients, found hexamethonium chloride to be an effective hypotensive agent, the action of which was sometimes augmented by hydralazine hydrochloride ("apresoline"). Work on the control of malignant hypertension has also been published by Page (1951).

Adverse views on the oral value of administration of methonium compounds have been given by Locket *et al.* (1951), whereas in the hands of Mackey and Shaw (1951) and Campbell *et al.* (1952) this method was effective. Kilpatrick and Smirk (1952) have found the oral route a useful substitute for injections, although the results were less predictable; oral therapy was more likely to be successful when the patient was sensitive to small subcutaneous dosage. Provided the adjuvant effect of a salt-free diet was remembered, and provided close and continued clinical observations were used to adjust dosage, they believed that the oral route could be valuable, especially when excretion was delayed, as in some cases of chronic nephritis.

Material and Results

The material for this survey comprised a group of 83 patients derived from hospital and private practice who have been treated with hexamethonium for hypertension in one hospital over a period of three years. The majority of these patients have been followed by us in a clinic reserved solely for patients with hypertension, and have been admitted from the clinic for 24-hour blood-pressure observations in the ward.

In the clinic, the blood pressure, in the lying and standing positions, has been taken independently by two observers. Routine sensitivity tests with hexamethonium showed that there was a definite postural hypotensive effect in all cases, whatever the sensitivity of the blood pressure to hexamethonium in the horizontal position. This postural effect persisted on exercise (Fowler and Guz, 1954) and was found to be an important factor in controlling the blood pressure. It was shown that hexamethonium could be used successfully irrespective of the original sensitivity test made in the lying position.

Severity of the disease was assessed on retinal and renal changes as well as on the height of the blood pressure, but details of the former have not been included. The blood-pressure figures presented below indicate that treatment for the main part was reserved for the most severe cases.

In Table I is shown the route by which hexamethonium was administered in 83 patients treated for hypertension. In addition, it shows that treatment had been abandoned

TABLE I.—*Treatment of 83 Hypertensive Patients with Hexamethonium*

Route	Treatment Continued	Treatment Abandoned	Total
Parenteral ..	35	16	51
Oral	25	7	32
Total ..	60	23	83

in a higher proportion (31%) of those treated parenterally as compared with those treated orally (22%). There were two reasons for this difference. First, there were more severe cases of hypertension in the parenterally treated group and more of these patients had died; secondly, it was unjustifiable to continue a remedy parenterally if it proved to be ineffective. Oral therapy was often continued with good symptomatic results in cases in which it was having little or no influence on the blood pressure.

Parenteral treatment was far more effective in controlling the blood pressure than oral therapy (Table II). In the cases with an initial diastolic blood pressure of 120 mm. Hg or

TABLE II.—*Comparison of Parenteral and Oral Treatment in Controlling the Blood Pressure in 60 Subjects with Different Initial Blood-pressure Levels, Still Under Treatment*

Range of Initial Diastolic B.P.	Control of Blood Pressure in										Total of All Cases
	Parenterally Treated Cases					Orally Treated Cases					
	Good	Fair	Poor	Nil	Total	Good	Fair	Poor	Nil	Total	
120 or less	0	1	0	0	1	2	2	1	4	9	10
121–140	9	8	9	1	27	1	2	3	4	10	37
Over 140	2	3	1	1	7	0	1	1	4	6	13
Total ..	11	12	10	2	35	3	5	5	12	25	60

less, oral therapy was effective in controlling it in half the cases treated. For the 13 cases with an initial diastolic blood pressure over 140 mm. Hg, control was fair or good in five out of seven treated parenterally, while for the orally treated cases in this group there was no effect on the blood pressure in four patients out of six. In this group of six orally treated patients with very high diastolic pressures the side-effects produced by effective therapy given parenterally were not tolerated by the patient or rigid control of the blood pressure was found to be contraindicated. Despite the poor blood-pressure control in this group of six cases with a high initial blood pressure treated orally, the symptomatic result was good in four cases, fair in one, and recorded as nil in a patient (Case 9) who presented with a monoplegia (Table V). The effect of leaving the blood

pressure uncontrolled in this group of cases cannot yet be assessed, as the patients have been under surveillance for too short a period for this purpose, the average duration of treatment for the group being a little over seven months.

It will be seen in Tables III, IV, and V that the symptomatic result of treatment bore no relation to the degree of blood-pressure control. When the patients presented with symptoms rather than complications of hypertension, there was uniformly satisfactory relief of these symptoms. Headache was the most distressing presenting symptom in 21 (25%) of the 83 cases (Table III). This Table included only those in whom headache was the most important presenting symptom, and by omitting those cases in which headache was an incidental or even a joint presenting symptom a more certain assessment of the relationship of headache to the level of blood pressure was made possible. As shown in Table III no relationship exists between the control of blood pressure and the relief of headache.

TABLE III.—*Control of the Blood Pressure and Relief of Headache in* 21 *Cases of Hypertension Presenting with Headache*

Control of Blood Pressure	Relief of Headache				
	Good	Fair	Poor	Nil	Total
Good	5	1	—	—	6
Fair	4	2	—	—	6
Poor	3	—	—	—	3
Nil	4	2	—	—	6
Total ..	16	5	—	—	21

In numerous papers on the subject of the treatment of hypertension with hexamethonium, full details are given about a few patients; it may not always have followed that these illustrative cases were the average response to treatment, although this is often the impression which the paper conveys. In our series there was an extraordinarily wide range of response to treatment. For this reason a précis of each case in our series which is still continuing treatment is given in Tables IV and V.

In 12 patients one injection only in the 24 hours was given, on retiring at night. These were patients in whom side-effects were marked and the prevention of heart failure, the most common termination of hypertension, was the dominant consideration in treatment. It is well recognized that the blood pressure in normal persons and in hypertension falls during sleep, and, if it were not for the practical consideration of avoiding unpleasant side-effects, a single injection given in the morning would be of more value in maintaining an even lowering of blood pressure. It appeared, however, that by using hexamethonium to lower the blood pressure during the night below the level reached by sleep alone the cardiac reserve was increased. The dose given in these cases caused no symptoms, as the injections were given just before retiring. The same dose given in the morning was found to be intolerable to the majority of these patients.

Duration of Treatment

As experience with hexamethonium therapy was gained, the oral route was used less often, and in all severe cases the attempt to control the blood pressure was made by using hexamethonium parenterally. Table VI shows that 32% of the patients still under treatment had been given hexamethonium for less than six months.

Those cases which had been treated parenterally for two years or more showed far more satisfactory control of the blood pressure than the group treated for less than six months. Clearly, as time went on, the less satisfactorily controlled patients would be taken off parenteral treatment, but failure to control the blood pressure was usually evident in the first six months of treatment. All 16 patients for whom parenteral therapy was abandoned were treated for under six months. Details of these patients are given in Table VII.

Side-Effects of Hexamethonium

Most of the side-effects are directly attributable to the ganglion-blocking action of this drug or to the fall in blood pressure.

TABLE IV.—*Parenteral Treatment with Hexamethonium Bromide in 35 Patients Continuing Treatment*

Case No.	Age First Seen and Sex	Presenting		Dose in mg.	Symptomatic Result	Control of Blood Pressure			
		Symptom or Condition	B.P.			Duration Treatment (Months)	B.P. Recording	Hours after Injection	Assessment of Control
1	49 M	Angina pectoris ..	210/130	100 b.d.	Good	24	175/100	7½	Good
2	59 M	Epistaxis	240/125	60 „	„	8	225/140	8½	Nil
3	40 F	Headache	230/130	100 „	„	24	180/110	7	Fair
4	39 F	„	230/120	120 nocte	„	6	180/100	16	„
5	53 M	Nil (life) later A.P. ..	285/125	100 „	„	12	220/115	16½	Poor
6	34 M	Headache	210/130	200 „	„	24	140/90	17	Good
7	53 M	„	220/140	60 „	„	6	170/120	17	Poor
12	52 M	„	220/130	60 b.d.	„	4	200/120	5	„
25	55 M	Hemiplegia	200/125	60 „	„	4	160/110	7½	Fair
26	53 M	Angina pectoris ..	220/140	100 „	„	24	155/110	4	
							175/110	7	Good
27	50 F	Headache	240/160	250 „	„	12	175/100	7½	„
31	60 M	Blurred vision ..	300/180	80 „	Fair	3	300/170	6	Nil
37	35 M	Lassitude	240/130	50 „	„	11	200/140	8	Poor
41	53 M	Congestive failure ..	200/140	50 nocte	„	10	130/90	6½	
							200/120	19	Fair
45	48 F	Precordial pain ..	250/140	100 „	Good	12	245/135	13½	Poor
49	34 M	Headache	280/180	150 b.d.	„	12	140/100	7	Good
50	55 F	Dyspnoea	260/145	60 nocte	„	4	130/110	1½	Fair
54	55 F	„	230/130	60 „	„	9	200/120	17½	Poor
59	36 M	Epistaxis	210/140	80 b.d.	„	10	175/115	7½	Fair
60	40 F	Angina pectoris ..	220/140	50 „	„	2	170/120	7½	Good
61	58 M	Dyspnoea	230/140	80 „	„	3	180/130	4½	Poor
62	46 F	Bilious attacks ..	250/140	100 „	„	1	200/130	5	„
63	56 M	Cerebral thrombosis	250/130	50 nocte	„	10	230/150	19	„
65	59 F	Headache	245/140	60 „	„	3	170/100	17	Good
66	58 F	Epistaxis	300/160	50 t.d.s.	„	10	200/130	3	Fair
68	48 M	Headache	220/125	60 mane 70 nocte	„	2	170/125	9	„
69	48 F	Dyspnoea	250/150	60 „	Fair	3	225/115	16½	„
70	61 F	„	250/130	60 b.d.	Good	1	200/115	7	„
71	37 F	Nil	235/130	80 „	N.A.	1	210/125	8½	„
72	66 M	Nearly blind	290/145	80 „	Nil	5	225/110	4½	Poor
76	60 M	Paroxysmal dyspnoea	210/130	70 „	Good	6	140/90	2	Good
77	36 M	Hypertensive encephalopathy	215/130	160 „	„	3	160/100	4	„
78	45 M	Severe dyspnoea ..	170/130	120 „	„	5	110/80	3	„
80	44 F	Congestive heart failure	210/130	100 „	Fair	6	150/100	3½	„
81	58 M	Dyspnoea	245/130	120 „	Good	1	170/100	4	Fair

TABLE V.—*Oral Treatment with Hexamethonium in 25 Patients Continuing Treatment*

Case No.	Age First Seen and Sex	Presenting: Symptom or Condition	Presenting: B.P.	Dose in Tabs. of H.M.B. or H.M.T.	Symptomatic Result	Blood Pressure Control: Months after Treatment	Blood Pressure Control: B.P.	Blood Pressure Control: Assessment of Control
9	55 F	Monoplegia	250/150	H.M.T. 4 t.d.s.	Nil	8	220/120	Nil
10	41 M	Headache	200/125	H.M.B. 4 „ H.M.T. 4 „ alt. weeks	Fair	15	150/95	Good
11	44 F	Dyspnoea	230/110	H.M.T. 4 t.d.s.	Good	12	240/110	Nil
16	45 F	Headache	260/170	H.M.B. 4 „	Fair	6	250/140	„
18	51 F	Anxiety neurosis	240/135	H.M.B. 1 b.d. (placebo)	Good	15	215/100	Poor (weight reduction)
19	59 F	Cerebral thrombosis	250/130	H.M.B. 2 t.d.s. H.M.T. 2 „ 2 wks. altly.	„	4	200/120	Fair
22	51 F	Headache	245/120	H.M.T. 3 t.d.s.	„	12	230/120	Nil
24	48 F	Angina pectoris	235/125	H.M.B. 2 q.d.s.	„	1	220/120	„
29	57 M	Headache	220/150	H.M.B. 2 „	„	10	230/140	„
30	52 F	Giddiness	230/130	H.M.T. 5 t.d.s.	„	24	240/115	Poor
34	54 F	Headache	210/130	H.M.B. 4 „	„	12	210/130	Nil
35	46 M	Retinal haemorrhage	190/120	H.M.B. 2 „	„	30	150/90	Good
40	62 F	„ „	200/120	H.M.T. 2 „	Nil	10	170/115	Poor
42	40 M	Headache	250/150	H.M.T. 2 „	Good	6	210/125	Fair
44	62 M	„	200/115	H.M.B. 2 „	Fair	15	150/110	„
46	52 M	„	210/150	H.M.B. 2 „ H.M.T. 2 „ 3 wks. altly.	Good	12	210/140	Nil
51	44 M	„	200/120	H.M.B. 1 t.d.s.	„	6	150/80	Good
52	43 F	Dyspnoea	190/120	H.M.B. 2 „ H.M.T. 2 „ 3 wks. altly.	Fair	8	185/130	Nil
53	57 M	Headache	240/140	4 H.M.B. 1 t.d.s.	„	12	220/130	„
55	43 F	Dyspnoea	195/130	H.M.B. 6 b.d.	Good	20	190/120	„
57	55 F	Lassitude	220/130	H.M.B. 2 t.d.s.	„	12	160/100	Fair
58	55 M	Visual disturbance	220/120	H.M.T. 2 „	Fair	24	220/130	Nil
73	35 F	Headache	200/120	H.M.T. 3 q.d.s.	Fair	18	175/100	Fair
74	45 F	„	245/150	H.M.B. 2 t.d.s. H.M.T. 2 „ 2 wks. altly.	Good	1	200/115	Poor
75	60 M	Left ventricular failure	180/130	H.M.B. 5 b.d.	Good	12	170/120	„

H.M.B.—Hexamethonium bromide. H.M.T.—Hexamethonium bitartrate.

TABLE VI.—*Correlation of Blood-pressure Control with Duration of Treatment in 60 Patients Still under Treatment*

Duration of Treatment	Control of Blood Pressure in: Parenterally Treated Group: Good	Fair	Poor	Nil	Total	Orally Treated Group: Good	Fair	Poor	Nil	Total
Under 6 months ..	4	7	4	1	16	0	1	1	1	3
6 months to under 1 year	2	4	4	1	11	1	1	1	4	7
1 year to under 2 years	2	0	2	0	4	1	3	2	6	12
2 years and over ..	3	1	0	0	4	1	0	1	1	3
Total ..	11	12	10	2	35	3	5	5	12	25

TABLE VII.—*Details of 16 Patients Treated Parenterally who Died or for Whom Treatment was Abandoned*

No. of Cases	Details	Result
5	Advanced cases of malignant hypertension, uraemia	All five died
3	Cardiac infarction: 2 developed after treatment was abandoned	Both died
	1 „ during treatment	Recovered
4	Cerebral vascular accidents: 1 thrombosis during treatment	Recovered
	1 „ after treatment abandoned	Died
	1 haemorrhage (presumed) during treatment	„
	1 „ (post mortem) „ „	„
4	Treatment abandoned because of side-effects	3 alive, 1 unknown

Effects Due to Fall in Blood Pressure

Postural Hypotension.—This has been regarded by some as an undesirable side-effect, but we have utilized it in treatment. Conway (1953) has shown that the fall of blood pressure in the horizontal position is unpredictable in hypertensive subjects and there is no fall of diastolic blood pressure in normal persons when lying horizontally. Work done at the Hammersmith Hospital on normal persons (Morrison and Paton, 1953) differs from Conway's findings only where the blood pressure was taken in the semi-recumbent instead of the lying position. The postural hypotensive effect is, however, constant. When treatment is started, postural faintness can be unpleasant, and, unless the patient is told to lie flat on recognizing this symptom, the natural reaction is to "walk it off." This may be ineffective and the patient lose consciousness. Later mild symptoms can and should be walked off.

Muscle Weakness.—True weakness of muscles is a common symptom when the blood pressure falls to a low figure in severe cases of hypertension. This effect is probably due to a temporary deficiency in the blood supply.

Angina pectoris and intermittent claudication are in some cases clearly related to the fall in blood pressure.

Lassitude and increased susceptibility to cold may occur in severe cases of hypertension rigidly controlled by hexamethonium bromide; these symptoms are often worse when the blood pressure is lowest. Raynaud's phenomenon developed in a patient with pre-malignant hypertension after the blood pressure had been adequately controlled for six months.

Effects Due Directly to Ganglion-blocking Action

Gastro-intestinal Disturbance.—Dryness of the mouth is a constant symptom at the start of treatment, but after a few months it distresses only the less stable patients. Alteration of bowel habit is more common with oral than with parenteral therapy. Constipation is rather more common than diarrhoea but easier to treat. In one case treatment was discontinued when the patient strangulated his hernia straining at stool.

Bladder Disturbance.—Slight difficulty in starting micturition was often experienced during parenteral therapy. One patient had relief of stress incontinence by the hexamethonium. Another patient, who received 250 mg. of hexamethonium bromide twice daily, developed complete retention after each injection for about ten hours and then suffered sudden urinary incontinence.

Paralysis of Accommodation.—This was met by prescribing spectacles to correct the visual disturbance for close work when under the influence of hexamethonium. This remedy was found to be effective.

Impotence.—This could be overcome by giving the evening injection at a later hour when necessary.

Discussion

The value of a remedy used for the treatment of hypertension might be gauged by the effect upon symptoms, by the control of the blood pressure, or by prevention of the complications of hypertension, and the consequent improvement in the expectation of life. These criteria are reviewed in turn.

1. Relief of Symptoms

Many symptoms are attributed to hypertension, of which only headache occurs with any consistency. It is common experience for the headache and other symptoms to develop for the first time after the patient knows that the blood pressure is raised. The symptoms of hypertension are relieved by any treatment if it is given with sufficient confidence and enthusiasm. There is no evidence that at the same time the expectation of life is increased or that the patient will be allowed to escape the complications of hypertension. Ayman (1930) clearly showed the effect of suggestion on the symptoms of hypertension by treating hypertensive patients with dilute hydrochloric acid by mouth, obtaining by this means excellent relief of symptoms and, with the lessening of anxiety, even some reduction in blood pressure. These findings were later confirmed by someone who misinterpreted his results to such an extent that by a peculiar process of rationalization he believed that hydrochloric acid was of intrinsic value, lowering the blood pressure by some chemical effect.

Stewart (1953) has made a careful study of headache in hypertension and produced convincing evidence to show that the headache is usually due to anxiety in subjects who know that their blood pressure is raised. He assessed the significance of headache in hypertension by comparing a group who knew they had hypertension with a group unaware that their blood pressure was raised. With the present material the relationship of headache to the raised blood pressure has been studied by comparing the relief of symptoms in patients grouped according to the degree by which the blood pressure is controlled with hexamethonium bromide. Using this technique to evaluate the significance of headache in hypertension, we agree substantially with Stewart's conclusions. Relief of anxiety when it was thought that the blood pressure was controlled caused disappearance of headaches and other symptoms. As Stewart observed, there are a few cases in which headache does appear to be a direct effect of the increased blood pressure, as in the following instance.

Case 37.—A man aged 36 presented with headaches, a feeling of tightness, and throbbing in the head. He was found to have severe essential hypertension with a blood pressure of 240/130. There were grade II changes in the fundi oculi and the left ventricle was moderately enlarged. The cardiogram showed left ventricular strain. The blood pressure was well controlled in hospital by hexamethonium bromide dissolved in polyvinylpyrrolidone 50 mg. subcutaneously, morning and night. When seen one month later in the out-patient department, he stated that for two hours after each injection he felt very weak, the eyes were blurred, and the mouth dry. The next two to three hours he felt very well, but then developed a headache which was "tight" and throbbing in character. When seen nine hours after an injection, at a time when the headache was becoming very severe, the blood pressure was 280/160.

It was thought useless to assess the value of hexamethonium bromide by the relief of those symptoms of which the hypertensive patients complain. However, if this criterion is used the results will appear to be very satisfactory. Relief of symptoms appeared to be greatest in those attending a clinic for hypertensive patients as compared with the remainder attending the general medical out-patient department. Although the relief of symptoms could not be correlated with the control of blood pressure, it was intimately related to the reassurance they obtained from the treatment. It would be surprising if any operation, confidently performed, for the relief of the symptoms of hypertension failed to succeed in this aim in the vast majority of cases.

2. The Value of Blood-pressure Control

It has often been stated in the past that artificial lowering of the blood pressure was an unwarranted interference with a necessary adaptation by which the tissues obtain a sufficient blood supply against an increased peripheral resistance. This was an assumption incapable of proof before an effective means of controlled blood-pressure reduction was introduced. In any large series of cases treated with methonium compounds there will now be examples that vividly illustrate the truth of this assumption under certain circumstances. A study of such material will also put this valid contention into its proper perspective.

In the present series 3 out of 83 patients suffered from the reduction of blood pressure; none died, and in each of them treatment with hexamethonium was abandoned.

In one instance (Case 32) a left hemiplegia occurred one hour after a subcutaneous injection of hexamethonium dissolved in water. The paralysed limbs made a slow but complete recovery. Later all cases were treated with hexamethonium dissolved in polyvinylpyrrolidone. In this way absorption from the subcutaneous depot is slowed and not only prolongs the action of hexamethonium but renders the fall in blood pressure less precipitous. Despite this modification of treatment a patient (Case 56) suffered a cardiac infarction one and a half hours after injection.

The third example clearly illustrates the need for a high head of pressure in some cases of hypertension. This patient (Case 13) was admitted to hospital with essential hypertension. Her blood pressure was satisfactorily controlled by two injections a day of hexamethonium bromide in polyvinylpyrrolidone subcutaneously. When followed up in the out-patient department she later complained of failing memory and mentioned that her speech became slurred two hours after an injection. It was now clear that she was suffering from the effects of progressive cerebral ischaemia, and treatment with hexamethonium bromide was therefore discontinued. Patients who show progressive cerebral ischaemia should not be treated with agents to reduce the blood pressure, but occasionally it may not be obvious that this process is taking place before treatment is instituted.

Despite the danger of precipitating thrombosis by lowering the blood pressure, the danger of a high blood pressure *per se*, regardless of aetiology, is a consideration of the greatest importance. We have found that, by the careful choice of patients, fluctuations in the blood pressure are not attended by a much-increased risk of thrombosis even when the blood pressure falls to a very low level, sufficient sometimes to cause loss of consciousness.

3. Prevention of the Complications of High Blood Pressure

While the reduction of blood pressure in hypertension is not without danger under certain circumstances, the changes that a marked elevation of blood pressure produces in the cardiovascular system inevitably threaten life.

Heart Failure.—The most common cause of death in hypertension is heart failure, followed by cerebral haemorrhage and thrombosis and then coronary artery disease (Bell and Clawson, 1928). Unless essential hypertension has entered the malignant phase renal failure is a very rare cause of death, in Christian's (1926) series making up only 4.5%. Although the development of heart failure may not be exactly related to the height of the blood pressure, the association is intimate. Since heart failure may for years be the only manifest complication of hypertension, and since it is the commonest cause of death, the effect of hexamethonium in preventing this complication is of major importance. In the treatment of incipient heart failure it

has already been shown to be of value, although in no way replacing treatment with digitalis and mercurial diuretics when these drugs are indicated. Kelley and his co-workers (1953) have claimed that congestive heart failure due to causes other than hypertension can be relieved by hexamethonium, and they have discussed the mechanisms by which this relief may occur. Further clinical studies on the cardiac reserve of our hypertensive patients treated with hexamethonium are in progress.

Cerebral Haemorrhage.—It is hoped that lowering of the blood pressure may lessen the chances of a cerebral haemorrhage occurring. Normal arteries can withstand enormous pressures without breaking—far beyond any levels obtaining in life (Lampert and Müller, 1926). It has been suggested that the danger of cerebral haemorrhage is related to a fluctuating high blood pressure (Westphar and Bär, 1926). If this is the case, it may be argued that hexamethonium bromide, even with its absorption delayed by polyvinylpyrrolidone, would cause the fluctuation in blood pressure which might precipitate a cerebral haemorrhage. On the other hand, it has been shown that the rise of blood pressure on exercise in the hypertensive person is lessened under the influence of hexamethonium bromide (Fowler and Guz, 1954).

4. Expectation of Life

At least ten years must elapse before any definite pronouncement could be made on the effect of blood-pressure control in prolonging life in benign essential hypertension. Final assessment of the value of hypotensive drugs in preventing the complications of hypertension must also await the passage of time in benign cases of the disease. In so-called malignant and pre-malignant hypertension, when the expectation of life is so short without treatment, a clear-cut assessment of the value of blood-pressure control should easily be made. In practice there are certain difficulties, of which the most important is the recognition of pre-malignant hypertension. Many of the so-called pre-malignant cases of hypertension which have done well on hexamethonium may have been misdiagnosed. Once renal failure has developed, lowering of the glomerular filtration pressure resultant on blood-pressure reduction may precipitate a terminal uraemia; but unless there is evidence of severe renal damage it is difficult to be certain that the prognosis without treatment is immediately grave.

Practical Aspects of Selection and Management

Experience gained while using hexamethonium in a clinic for hypertension has convinced us that this drug has a definite part to play in the control of a selected group of hypertensive patients.

As a method of controlling the blood pressure hexamethonium compares favourably with sympathectomy. A drawback in severe cases of hypertension is the necessity for repeated subcutaneous injections, for even in patients who are obviously benefiting from their treatment it may be difficult to persuade them to continue injecting themselves for more than a few months. When it is judged that continued treatment is of value it may be useful and fair to liken the patient's state to that of the diabetic patient with his insulin. Many practitioners have believed that hexamethonium therapy is too complicated and hazardous for them to undertake, and one of the purposes of the present paper is to try to show how the medical attendant can continue the management of these patients.

Indications

The indications for treatment with hexamethonium bromide are for the relief of symptoms either in the presence of high blood pressure or in those cases where the blood pressure in itself is constituting a definite peril to the patient. In the former category may be placed the acute episodes of left ventricular failure, eclampsia, and hypertensive encephalopathy, together with the chronic disorders of benign and malignant essential hypertension and certain cases of renal hypertension in which renal function is still adequate. In the latter category it is difficult to stipulate what degree of sustained hypertension constitutes a more than average menace to life; the level of the blood pressure must be taken in conjunction with retinal, urinary, cardiographic, and radioscopic findings, but in this series it has been felt that the administration of hexamethonium should be seriously considered in all cases with a diastolic blood pressure of 130 mm. Hg or more.

On the whole hexamethonium treatment has been reserved for the younger hypertensive patients in this series and certainly those under 60 years of age, when there is less chance of gross arterial disease being present. A previous cerebral or coronary thrombosis is not a contraindication, but special caution is needed in lowering the blood pressure in such cases. Similar reserve should be shown in the use of hypotensive agents in the presence of anginal symptoms or when there is cardiographic evidence of myocardial ischaemia. Renal failure with a rising blood urea is an absolute contraindication to hypotensive therapy, which only aggravates the situation by impairing renal function still further.

Route

In common with most other workers we have found that the only reliable route for administration of hexamethonium compounds is the subcutaneous one. This does not preclude the use of oral preparations in milder hypertensive patients or in individuals intolerant to other routes. Absorption is variable, however, and Harington (1953) has found that this amounts to no more than between 1% and 6% (depending on the preparation) when taken after food, though if administered when fasting the percentage may be as high as 40. The bitartrate compound introduced in order to obviate the danger of bromism is particularly unsatisfactory in this respect. The variable absorption of oral preparations may lead to sudden severe side-effects such as paralytic ileus and irreversible hypotension. Nevertheless, satisfactory symptomatic results were obtained using oral therapy. It might be argued that an inert tablet would be equally successful and less unpleasant from side-effects, but it would seem that in a certain group of patients oral hexamethonium bromide is controlling the blood pressure when a fall in the level is more than can be accounted for by the relief of anxiety. In the main, however, oral therapy was reserved for the milder cases or even as a placebo measure, severe hypertensive patients, and in particular those in a malignant or pre-malignant phase, being treated, with rare exceptions, by the parenteral route. Oral and parenteral routes may be combined as a nightly injection with tablets during the day.

Routine

The routine treatment adopted in the present series consisted of two or three subcutaneous injections of hexamethonium bromide daily; the watery solution was used in the earlier cases, but later all patients were treated with a delaying preparation (hexamethonium bromide in polyvinylpyrrolidone). In addition further delay was attained by including a small dose of ephedrine (0.5 mg. in 0.1 ml.) added to the dose in the syringe, but the retardation was found to be only slight, and its addition was reserved for the more intelligent patients. Every patient under treatment had the head of the bed raised on 9-in. (23-cm.) blocks.

A nightly injection technique was reserved for two groups of cases. (1) Those in whom side-effects were so marked after an injection that their daily life was made miserable. With one injection on retiring, the side-effects were lost in sleep and had disappeared on rising in the morning. (2) Less severe cases of hypertension, in which the clinical picture clearly indicated that cardiac failure rather than any other complication of hypertension was imminent.

In practice, treatment with a single daily injection has in some cases appeared to be beneficial, and over the months the exercise tolerance has improved even in patients who had in the past been in cardiac failure. In one patient,

however, receiving injections twice daily, left ventricular failure supervened as the fluctuating blood pressure started to rise.

Case 78.—A 48-year-old man with previous symptoms of left ventricular failure which had been adequately controlled by digitalis, diuretics, and salt restriction was started on hexamethonium treatment by subcutaneous injection twice daily. While still under in-patient observation he began to experience the early symptoms of pulmonary congestion nine hours after each injection, with greatly increased dyspnoea and dry cough. These symptoms would subside rapidly after the subsequent injection.

After admission to hospital and the usual routine clinical examination with investigations to exclude underlying causes for the hypertension, a decision was made regarding the need to control the blood pressure with hexamethonium bromide. Although the indications for blood-pressure control have been broadly stated, more emphasis has been laid on signs rather than symptoms in assessing the need for treatment.

It was felt that too much emphasis has been placed on the resting blood pressure. There can be little relation between the artificially low blood pressure reached by weeks of bed rest with sedation and the blood pressure during the activities which the patient with hypertension is normally allowed to carry out. When the patient is seen later in the medical out-patient department there can be no comparison between the blood pressures recorded there and the figure reached after prolonged bed rest in hospital.

The majority of patients in this series have been followed up after discharge in a clinic for hypertension. Once stabilized they attend the clinic at two- to three-monthly intervals, bringing their night apparel, so that they can, if necessary, be admitted for 24-hour blood-pressure observation.

Changing Sensitivity to Hexamethonium

As treatment is continued, both the blood-pressure response to hexamethonium bromide and the side-effects of the drug undergo changes. Patients often develop an increasing tolerance for the first ten days of treatment, but this is by no means invariable. During this time side-effects abate in parallel with the rising blood pressure. Later the sensitivity to hexamethonium bromide varies in an inconstant way and sensitivity to the drug may increase; this is especially common during the first six months. It is therefore not only necessary to see these patients at frequent intervals but also to admit them for 24-hour blood-pressure observation. Side-effects at this stage of treatment tend to become less severe even when the blood pressure continues to be satisfactorily controlled, but new symptoms due to the ganglion-blocking action of the drug may arise *de novo* at any time. No way of predicting the response to treatment with hexamethonium bromide could be found, and even the hexamethonium sensitivity test done before the start of treatment was of little value in forecasting the effect of therapy.

Continuation Treatment

Although the use of hexamethonium bromide is indicated for the control of an appreciably raised blood pressure in the presence of symptoms, if the blood pressure remains uncontrolled with adequate treatment and side-effects are present no attempt to persist with the drug should be made.

Successful treatment of pre-malignant hypertension in favourable cases does not depend on specialist knowledge of the drug, but follows painstaking observations and repeated blood-pressure recordings while the patient is under treatment. Observation of renal function at the onset of treatment necessitates hospital supervision, but later the patient's doctor, if he has the time, is the best fitted to carry out the treatment. Initially hexamethonium bromide may be given eight-hourly or even more often to ensure adequate and smooth control of the blood pressure. On discharge from hospital the patient should be stabilized on injections given every 12 hours. The dose should be increased cautiously by not more than 10 mg. at a time. It is best done by increasing the evening injection alone for a few days, so that any unpleasant effects from the increased dosage may be lost in sleep, before increasing the morning dose.

Hexamethonium bromide is not the ideal treatment for hypertension, but is at present the most effective means of controlling the blood pressure. Despite reports of new allied compounds which are supposed to possess advantages because of their more selective sympathetic-blocking action, these claims have, for the most part, been based on rather crude experiments. It seems unlikely that this series of ganglion-blocking agents will possess appreciable differences in regard to their site of action, although their potency may vary. It also seems that changes in the structure of the methonium compounds to make them more easily absorbed from the bowel render them less effective ganglion-blocking agents. Since these compounds are excreted by simple glomerular filtration there is no way by which renal excretion can be delayed.

A more effective treatment for hypertension is needed. At the present time, however, the methonium compounds afford the only effective method of blood-pressure control in a proportion of hypertensive patients.

Patients with significant grades of hypertension should not be deprived of the benefit which can be conferred by hexamethonium treatment, a therapy which at best may transform the health of the patient, and at worst may only have to be discontinued.

Summary

Hexamethonium bromide has been used in the treatment of 83 hypertensive patients who have been followed up over periods varying from six months to three years.

In all instances treatment was initiated in hospital. It was found that hexamethonium bromide might be used successfully even when a sensitivity test is unfavourable. Patients continued this treatment at home with self-administered twice-daily injections, using the delayed-action hexamethonium bromide. After several weeks most were readmitted for a 24-hour blood-pressure survey. In some cases oral treatment by hexamethonium bitartrate was substituted for one or both injections.

Parenteral treatment was far more successful in controlling blood pressure than oral therapy, especially in those patients with the highest initial diastolic pressure. The blood-pressure control was good or fair in 66% of all those continuing parenteral treatment, as compared with 36% of those on oral therapy.

The effect of hexamethonium treatment in relieving symptoms bore no relation to the degree of blood-pressure control. When patients presented with symptoms rather than the complications of hypertension relief of symptoms was uniformly satisfactory. Headache was the presenting symptom in 25% of the 83 cases.

In 12 patients only one injection was given in the 24 hours, on retiring at night. These were patients threatened with left ventricular failure. They benefited by the several hours of lowered pressure through the night and at the same time were spared the side-effects often experienced soon after an injection.

During the course of parenteral treatment nine patients died and in six others treatment had to be abandoned for various reasons.

The side-effects from this treatment have been classified as those due to the fall in blood pressure and those directly due to ganglion-blocking action. Means of relieving such side-effects have been described.

The value of a remedy for hypertension has to be judged by (1) its control of the blood pressure, (2) the relief from symptoms, (3) the prevention of complications, and (4) the consequent improvement in survival time. These criteria have been discussed in the light of the results obtained.

The indications for treatment by hexamethonium bromide are as follows: sustained essential hypertension with a diastolic pressure at 130 mm. Hg or more; patients aged up to 55 or 60; progressive increase in blood pressure; threatening left ventricular failure due to hypertension; severe symptoms, notably headache and incapacity for work; threatened change from benign to malignant hypertension.

Contraindications were: blood pressure lower than the critical diastolic level mentioned above; age of 60 or over; evidence of more than slight impairment of renal function; evidence of more than slight cerebral or coronary disorder. While a reduction of pressure might be undesirable in these two groups, it must be remembered that continuing high pressure may equally, and perhaps earlier, bring serious hazards.

The practical application of these methods of selection and of treatment have been described with particular reference to treatment at home and at work.

For a substance to be accepted as a useful remedy for a disease so widespread and protracted as hypertension it must be available for use and control by the general practitioner. After the initiation of treatment the most important share in the control and management must be in his hands.

The possibilities, methods, and effects of oral therapy have been discussed.

While hexamethonium is not an ideal treatment for hypertension it is at present the most effective means of controlling high blood pressure. The risks of continuing high pressure far outweigh the possible danger from sudden fall of pressure.

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THE MEDICAL TREATMENT OF HYPERTENSION*

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The survey by Master *et al.* in 1943 showed that 30 to 40% of subjects over 40 years of age, and 65 to 75% of those over 70, have hypertension. It is well recognized that the prognosis is good in the majority of cases, but in many instances hypertension is followed by an increasing degree of disability which merits active therapy. The fact that hypertension, in itself, is often compatible with a normal life expectation tends to obscure its high mortality in those who develop symptoms. In his study of one thousand patients, Bechgaard (1946) found that 41% of males and 22.4% of females died within five to ten years of the onset of symptoms.

It is essential to have an acceptable definition of hypertension. Wood (1950) has defined the limits of normal blood pressure as 145/90 mm. of mercury, stating the precautions necessary in recording this. Systolic hypertension in the young is usually a response to emotion and exercise; in older subjects it is an indication of loss of elasticity of major arteries, and there are other causes. In essential hypertension it is the increase in the diastolic blood pressure which is significant, and this is the pressure to which reference is made subsequently in this review. In our survey we have examined patients presenting with a diastolic pressure of 100 mm. and over. Four years ago a new drug, hexamethonium, was placed at our disposal, and for the first time we had a reasonably certain method of reducing the level of the diastolic pressure to an extent greater than with general methods of treatment. It is therefore opportune to review our experience with hypertension over these four years, having particular regard to its treatment.

It is of interest to attempt to correlate the manifestations of hypertension in man with experimentally induced hypertension. Page (1949) has comprehensively reviewed the methods of production of hypertension in animals. The types of greatest interest in relation to the pathogenesis of hypertension in man are the hypertension which follows renal ischaemia and that resulting from administration of D.C.A. (deoxycortone acetate). The renal ischaemia experiments are based upon the work of Goldblatt *et al.* (1934), and implicate a humeral pressor mechanism. Wilson (1953) has examined the renal factors. It is possible that the mechanism of renal ischaemia, with its vicious circle of hypertension and further renal damage, operates in malignant hypertension.

In studying the basophil adenomata of the pituitary, Cushing (1932) recorded observations which have been followed by the implication of pituitary and adrenal factors. Merrill (1952) has been concerned with the adrenal mechanism, suggesting a psychic origin of stress

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and anxiety, with resulting excess of steroids. His hypothesis is illustrated in Table I. Wolferth *et al.* (1951) believe that the adrenal cortex is more fundamental in the maintenance of hypertension than the sympathetic nervous system. Studies upon the experimental production of hypertension will elucidate the basic aetiology of the disease, but experimentally induced hypertension in animals fails in many respects to parallel the disease in man.

TABLE I.—*Psychomotor Mechanism of Hypertension (after Merrill)*

Psychic stimuli	Adrenal cortical hormones	Renal tubule handling of Na. Relation to renal pressor mechanism. Direct pressor effect.
	Adrenal medullary hormones	Increased cardiac output. Direct vasopressor effect. Relation to cortical hormone.

Incidence of Hypertension

Medical Out-patients

During the four-year period 1950–3 4,872 persons were examined for the first time in the out-patient dispensaries of the Royal Alexandra Infirmary, Paisley. Of these, 841 were found to have a diastolic blood pressure of 100 mm. or over, with minimal to severe symptoms and signs of hypertension. There are several methods of ascertaining the severity of hypertension. The commonly used classification is the four groups described by Keith *et al.* (1938). It suffers from the limitation of being based upon the retinal changes. For the purposes of this survey it was decided to classify the patients according to the degree to which they were incapacitated by hypertension, not taking into account the level of the blood pressure. This grouping parallels the one proposed by the New York Heart Association for the classification of disability due to lesions of the heart. Upon a clinical assessment, our patients were graded as follows: — *minimal:* those having no symptoms referable to their hypertension, or symptoms such as headache which produced no incapacity; *slight:* those presenting with slight dyspnoea on exertion and a tendency to early fatigue; *moderate:* those whose activity was definitely restricted by fatigue and breathlessness on exertion; and *severe:* those with severe incapacity due to hypertensive cardiovascular changes.

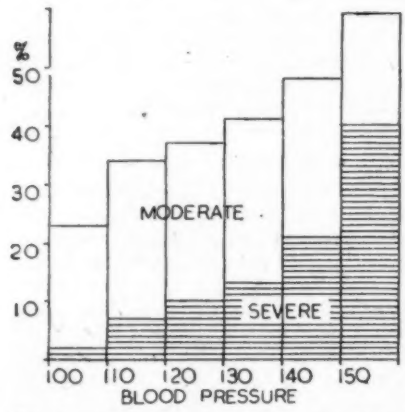

FIG. 1.—Percentage incidence of moderate and severe incapacity due to hypertension in decades of diastolic blood pressure.

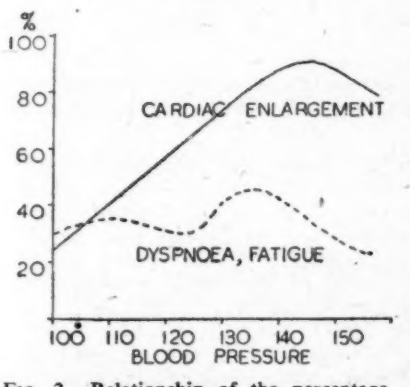

FIG. 2.—Relationship of the percentage incidence of dyspnoea and fatigue, and cardiac enlargement, to the diastolic blood pressure.

Fig. 1 shows the progressive incidence of severe incapacity in each decade of diastolic blood-pressure elevation. However, the marked variation in individual response to hypertension is shown by the relatively constant incidence of moderate incapacity, which is paralleled by the frequency of slight and even minimal disability. The number of patients seen who had hypertension increased with age, the maximum being at 55 years, with attenuation thereafter by death. In Fig. 2 the percentage incidence of cardiac enlargement and of the symptoms, dyspnoea and fatigue, has been related to the diastolic pressure, and it will be seen that the incidence of these symptoms bears no definite relationship to the degree of hypertension present, while the incidence of cardiac enlargement demonstrated radiologically increases with the hypertension. Severe incapacity is found with an increasing frequency corresponding to the elevation of diastolic pressure, and it is accompanied by an increasing incidence of cardiac enlargement. The incidence of dyspnoea and fatigue is not related to the degree of the hypertension.

Medical In-patients

There were 5,794 patients admitted for treatment during this period; of these, 564 (190 males and 374 females) were admitted on account of hypertension, their distribution in grades of incapacity being as follows:

Grade of Incapacity	Males	Females
Minimal	10%	10%
Slight	27%	33%
Moderate	45%	42%
Severe	18%	15%

The percentage incidence of the presenting symptoms and signs is shown in Table II. Dyspnoea and fatigue are the commonest symptoms, and the figures are similar to those for cardiac enlargement. In accordance with the experience of Frant and Groen (1950), cerebral accidents were commoner in the female (27%) than in the male (18%), while congestive failure was commoner in the male (24%) than in the female (17%). Obesity was found in equal numbers of males and females under the age of 40; it was twice as common in females aged 40–50, and three times as common in the over-50 group. Information was obtained upon the progress of 77% of patients following discharge: 47% of males died at an average of 19 months after leaving hospital and 35% of females died at an average of 23 months; cerebral vascular accidents accounted for 30% of female deaths and 19% of male deaths; heart failure was more common in males (44%) than in females (35%); renal failure occurred in 13% of the males and 14% of the females. Of the patients admitted for treatment for hypertension, 179 were treated by ganglion-blocking agents, comprising hexamethonium and drugs of this type.

TABLE II.—*Percentage Incidence of Symptoms and Signs in Patients Admitted for Treatment of Hypertension*

	Males	Females
Symptoms:		
Dyspnoea and fatigue	71%	81%
Headache	30%	51%
Chest pain	12%	13%
Signs:		
Cardiac enlargement	73%	82%
Cerebral accidents	18%	27%
Congestive failure	24%	17%
E.C.G. left ventricular preponderance	54%	58%
Fundi, grade II and III	87%	83%

Methods of Treatment

The methods of treatment of hypertension should be related to what is known of the aetiology and the experimental production of this disease. It is essential to give consideration to the prognosis in untreated hypertension. This has been reviewed in the *Lancet* (1953). Leishman (1953) has suggested subdivision of non-malignant hypertension into a benign form and an accelerated form, in which deterioration is slower than occurs in malignant hypertension. The rate at which the blood pressure rises is regarded by McMichael (1952) as being more significant than the height of the blood pressure. Our clinical experience suggests that *the development of symptoms and signs appears to be mainly due to the ability, or otherwise, of the individual patient's cardiovascular system to sustain the load of*

the hypertension. High levels of diastolic pressure are compatible with slight or even minimal incapacity in the individual. In essential hypertension it is probable that elevation of the diastolic pressure is compatible with a reasonable prognosis, except when signs and symptoms of heart failure appear. Headache, as Stewart (1953) has found, is a symptom which is probably unrelated to the severity of the hypertension. Renal involvement and cerebral vascular disasters occur, as a rule, late in the disease, and are not amenable to other than palliative treatment.

While the onset of heart failure constitutes a cardinal indication of the need for active therapy, the factors leading to the hypertension itself require study. A rise in the systolic pressure, accompanied by moderate elevation of the diastolic pressure of the order of 10 to 20 mm., tends to occur as the arteries harden with age. To some extent this finding has biased observations upon the prognosis of hypertension. The studies which have been performed are of relatively short duration, and systematic observation over a long period is required. Acceptance as physiological of an increasing diastolic blood pressure with advancing age is probably unjustified, in that Kean and Hammill (1949) have shown that among primitive peoples this does not occur, hypertension being associated with stresses encountered in civilized life.

Mental and Physical Stress

Graham (1945) has noted that, under the stress of prolonged periods of desert warfare, transient rises of pressure occurred, and Gavey (1954) has suggested that, under conditions of long-continued stress, the hypertension may become fixed. Wolf *et al.* (1948) and Gressel *et al.* (1949) have indicated that hypertensive vascular disease may be associated with obsessive compulsive traits and subnormal assertiveness, leading to an attitude of restrained aggression to the threats and challenges of everyday life, the vascular component of which comprises an elevation in the blood pressure and renal vasoconstriction. The study by Platt (1947) has confirmed that there is a marked hereditary predisposition.

Implication of a stress mechanism is strongly suggestive of a close parallel with the D.C.A.-induced hypertension in the animal, and with the hypertension of Cushing's syndrome. In recent years this has led to attempts to control hypertension by adrenalectomy. The results of this operation have been unsatisfying, and it is often combined with subtotal sympathectomy. Bowers (1954) has suggested that subtotal adrenalectomy should be restricted to malignant hypertension which cannot be controlled by medical therapy, chronic hypertension with marked organic changes, and Cushing's syndrome. Jeffers *et al.* (1953) performed a total or subtotal adrenalectomy with a modified Adson type of sympathectomy in 99 patients with severe hypertension. In 23% the response was excellent; in a further 23% a fair response was obtained; the response was poor in 30%; and 24% died post-operatively. The indications for adrenalectomy are therefore limited.

Dietary Restrictions

A less active approach on the adrenal mechanism is made by restriction of dietary sodium intake, and to this the Kempner (1948) rice–fruit–sugar diet owed part of its success. Schroeder *et al.* (1949) have concluded that the rice diet itself is of questionable value, but it is low in protein and very low in salt content; furthermore, it had a strong psychotherapeutic influence. The value of a diet containing sodium chloride in low daily intake of 0.5 to 2 g. is demonstrable, and its combination with a low-calorie intake is desirable. Martin (1952) has shown that reduction in obesity does not produce a significant fall in the diastolic pressure, but Fishberg (1937) has stated that reduction in dietary intake is followed after a week or two by a fall in the basal metabolic rate, and maintenance of this at a lower level reduces the load upon the heart to an extent which permits of an adequate control of the signs and symptoms of many patients with moderate elevation of the diastolic pressure. The milk diet introduced by Karell (1866) is initially very useful, and after a period of 72 to 96 hours this can be followed by an 800-calorie diet, the sodium content of which should be under 2 g. Reducing diets of this type are specially indicated in the obese, and they are of value in all cases of hypertensive heart failure.

Relief of stress is an important part of treatment, but in many cases it may be impractical to prescribe an alteration in the patient's activities or environment. Where hypertensive incapacity is severe, bed rest is essential. It is necessary to relieve any degree of anxiety from which the patient may suffer, and sedation will depress the psychic stimuli which Merrill (1952) has indicated. In out-patients phenobarbitone in dosage of up to 1 gr. (65 mg.) thrice daily can be prescribed, and for in-patients we have used sodium amytal in dosage of up to 3 gr. (0.2 g.) thrice daily.

A further factor of potential importance in the treatment of hypertension is the occasional occurrence of primary renal disease, due to chronic infection or to renal anomaly. Unilateral renal disease has not been encountered during our survey, and although Pickering and Heptinstall (1953) have recorded successful results following nephrectomy, Smith (1948) has concluded that nephrectomy should be restricted to the relief of definite unilateral renal disease amenable to operation, and not performed with hypertension as the indication. In advanced hypertension nephrectomy may actually shorten life by reducing still further the remaining functional renal tissue.

In summary, the general measures of treatment consist in relief of stress due to anxiety and environment, using sedation to assist in this, and treatment of heart failure by rest and restricted-sodium, low-calorie diets.

Reduction in the Level of Blood Pressure

The general methods of treatment are directed to modification of the circumstances which have occasioned the hypertension and reduction of the load placed upon the heart. In that the cardiovascular changes are due to the elevated blood pressure, there is an obvious necessity to use the means at our disposal to lower this. White (1947) lists many of the preparations previously used.

Synthetic Ganglion-blocking Agents.—(*a*) *Hexamethonium:* During a search for synthetic curarizing agents, Paton and Zaimis (1949) found that the sixth member of the methonium series of compounds (hexamethonium) possessed a marked and selective action in blocking the ganglionic synapse of the autonomic nervous system, and Arnold and Rosenheim (1949) demonstrated that the relaxation of sympathetic tone which is produced by this drug in man is followed by arteriolar dilatation, with reduction in the peripheral resistance. This occasions a pronounced fall in the blood pressure in both normotensive and hypertensive patients. Hexamethonium has been used extensively to decrease the blood pressure of patients with signs and symptoms of hypertension, and the results of treatment have been reviewed by Campbell *et al.* (1952), by Shaw (1952), and by many others. (*b*) *Pentolinium tartrate* (pentapyrrolidinium; "ansolysen"); Maxwell and Campbell (1953) have described a search for improved synthetic drugs, which resulted in the selection of a homologue of hexamethonium, pentolinium, as offering some advantages over hexamethonium. Smirk (1953a) has confirmed these findings.

Hexamethonium, its homologues, and compounds of this type are characterized by their ability to produce an immediate and usually marked fall in the blood pressure, the extent of which is dependent upon the dosage used and the individual degree of susceptibility of the patient. Side-actions occasioned by unselective ganglionic blockage are to be expected, and consist in constipation, dryness of the mouth, and blurring of vision. Tolerance develops quickly, so that dosage has to be increased to a maintenance level. The degree of control of the blood pressure attained varies from patient to patient, and oral dosage is useful in a proportion of patients only, since absorption from the gut tends to be variable.

Hydralazine (" *Apresoline* ").—This drug is said to have a central action upon the hypothalamus, and produces peripheral vasodilatation by a partial blocking action of adrenaline and noradrenaline. Its action has been studied by Schroeder (1952a), Hafkenschiel and Lindauer (1953), and others. The action of hydralazine is slower than that of hexamethonium, and, as its sites of action are different from those of the latter drug, combination of the two has been found to be of value. As has been reported by Schroeder (1952a) the side-actions are tachycardia, headache, vertigo, and nausea and vomiting. They tend to disappear as treatment is continued. In our limited experience we have not been impressed by the activity of hydralazine in comparison with that of hexamethonium, and have not therefore used this drug in treatment.

Veratrum Alkaloids.—The alkaloids of *Veratrum viride* produce a fall in the blood pressure which is probably due to a central action, and is accompanied by a bradycardia due to stimulation of the peripheral vagal nerve endings. Wilkins *et al.* (1949) and others have used this drug in the treatment of hypertension. It is available in this country as " veriloid." Mills and Moyer (1952) have found that the hypotensive dose closely approximates to the toxic dose which produces vomiting. They noted that this prevents effective use in the treatment of hypertension, and they prefer hexamethonium.

Hydrogenated Alkaloids of Ergot.—In contrast to the natural alkaloids of ergot, which cause contraction of smooth musculature and vasoconstriction, certain dihydrogenated alkaloids occasion peripheral vasodilatation and block adrenergic stimuli. This has been described by Rothlin and Cerletti (1949). They are available in this country as " hydergine." The action of these alkaloids in the control of hypertension described in the literature is unpromising, and limited personal experience has tended to confirm this.

Rauwolfia serpentia.—An alkaloid was extracted from this tropical shrub by Müller *et al.* (1952). Its action is said to be central, and it tends to produce a subjective improvement. The effect on the blood pressure is minimal, but it is free from side-actions. It is possible that it may be useful as an adjuvant to more active forms of therapy. The pure alkaloid is available as reserpine (" serpasil "). It is combined with veratrum alkaloids in the preparation of " rauwiloid." It is probable that it will be used in combination with hexamethonium. Wilkins *et al.* (1954) have reported favourably on this drug.

Indications for Treatment

Group I.—In view of the favourable prognosis in asymptomatic benign hypertension, no active treatment appeared to be indicated in most of those patients. A few patients presented with pressures over 120 mm. (below the age of 40) and over 140, and lowering of such pressure levels was attempted, together with close observation.

Group II.—Slight breathlessness on exertion and a tendency to early fatigue responded well to reassurance and sedation, with some restriction of activity.

Groups III and IV.—Moderate and severe incapacity required active treatment in hospital with the general measures outlined earlier. Of the patients in these groups, 149 were treated, in addition, with methonium compounds. The total of 179 patients treated with methonium compounds includes those in the first group and 14 cases of malignant hypertension noted subsequently.

There were two indications for the use of methonium compounds: (1) The presence of moderate or severe incapacity, and failure of the pressure to fall below 100 mm. within a fortnight or more in response to general measures of treatment. The range of initial pressure levels varied widely in the groups, as hypertension tends to be reduced when failure occurs. In the moderate cases the pressure was often labile, responding well to rest and sedation during the first admission, but within months or years the hypertension became fixed, so that subsequently methoniums became indicated. (2) High levels of pressure, usually in excess of 140 mm., accompanied by acute complications such as blindness, encephalopathy, and heart failure, constituted an indication for immediate dosage with methonium compounds.

Response to Treatment

Severe symptoms and signs of hypertension were improved by reduction in the blood pressure, and we have analysed the results obtained with methonium therapy (Campbell *et al.*, 1952). Similar results have been recorded by many others. While it is possible to effect reduction to normal pressure levels in almost every in-patient, subsequent observation generally shows a rise of pressure approaching the untreated level. However, it has often been observed that a fall occurs if the patient is again admitted or is adequately rested. *Methonium therapy tends to restore the lability of diastolic pressure.*

In 60% of the patients intermittent oral dosage with hexamethonium bitartrate in amounts totalling 0.75 to 2 g. of cation a day has been adequate to control signs and symptoms; a further proportion have required parenteral injection of this drug in quantities of up to 300 mg. of cation total a day. In common with Smirk (1954), we have not been able to ascertain whether treatment has extended the life expectation, but restoration to activity approaching normal has often been achieved during the period of survival. Pentolinium has provided a more certain method of lowering the blood pressure. A total dosage of up to 150 mg. of cation parenterally has been applied, and 1,000 mg. orally in some cases. The retard preparation described by Smirk (1953b) has been found valuable in reducing the number of injections necessary to one or two a day. During treatment with hexamethonium wide variations in pressure are often recorded, with fluctuations due to emotion. The pressure levels during pentolinium therapy are more stable. This is probably due to the greater effect of this drug upon the sympathetic nervous system than upon the parasympathetic. Pentolinium has proved much more certain in action, and in no case has a significant fall in blood pressure failed to occur following adequate dosage.

Malignant Hypertension

Fourteen patients presented with malignant hypertension: in seven there were no signs or history of previous hypertension; the others had hypertension of long standing which had entered into a malignant phase.

Malignant Hypertension of Recent Origin.—Three patients had chronic nephritis, and when first observed had gross impairment of renal function, with uraemia. Four patients had no previous history of renal disease, renal function was good, and blood urea was low during initial investigation, suggesting a diagnosis of primary malignant hypertension. Impairment of vision was a frequent symptom. Examination of the fundi showed fresh haemorrhages, and woolly exudates with frank papilloedema. No cardiac enlargement was present. The average diastolic pressure level was 140 mm. The duration of life was greater in those with chronic nephritis, extending from twelve days to four years, than in those with primary malignant hypertension, who died in from eight to nineteen months. Uraemia was progressive in all cases, as was a severe hypochromic anaemia.

Malignant Phase of Hypertension.—This occurred in older patients who had a history of hypertension of at least several years' duration. Impairment of vision was less commonly complained of, the presenting features being breathlessness on exertion and fatigue. Cardiac enlargement was present in all cases. The blood urea was either normal or but little raised, except terminally in one patient. Anaemia did not occur. Fundal examination showed sclerotic changes in the retinal arteries, old waxy hyaline exudates, and chronic retinal and disk oedema; fresh haemorrhages and exudates were superimposed. The prognosis was much better in this than in the previous group, five of the seven patients being

alive after eight months to four years. One woman died from a cerebral haemorrhage, and one man from uraemia.

As is described by Hadfield and Garrod (1947), a sudden rise in blood pressure causes arteriolar necrosis, in contrast to the fibrous thickening in the vessel walls which occurs in essential hypertension. In the first group extensive arteriolar damage occurred, particularly in the retina and the kidney. In the second group the arterioles were thickened to withstand chronic hypertension, and the subsequent changes were less severe.

Ganglion-blocking agents produced a fall in pressure to normal levels, with a dramatic improvement in the symptoms and signs in the 12 cases treated. Effective control of the pressure was not obtained after discharge of these patients from hospital, due to causes such as postural hypotension, constipation, vomiting and diarrhoea, blurring of vision, and, in some instances, discontinuance by the patients themselves of treatment. Even when full dosage was used the natural tendency of the patient to return to normal activity was followed by a rise in the pressure level. In the later stages control in hospital of the pressure level failed to arrest deterioration. However, regression of symptoms and signs of the malignant phase of hypertension was obtained more readily, with a probable extension of life.

Discussion

The marked improvement in the symptoms and signs in patients with hypertension which follows the application of general measures of treatment with and without ganglion-blocking agents has led us to adopt the hypothesis that control of the pressure level will return those patients to the category of asymptomatic hypertension, the prognosis of which is good. It has seemed reasonable to adopt measures which produce only a moderate reduction in the diastolic pressure level, as, from observation, the actual level is of less importance than the individual response to it. The period of observation has been inadequate to decide whether this symptomatic approach to treatment has increased or has failed to extend the expectation of life. However, observation of a few patients with hypertension in acute form, malignant hypertension, suggests that maintenance of the blood pressure at a level approaching normal—for example, under 100 mm.—is probably desirable in a proportion of individuals if the life expectation is to be increased. We have found that a marked reduction is not well tolerated by patients who have been accustomed to hypertension of several years' duration. Schroeder (1952b) has observed that this period of discomfort and loss of energy is transient, adaptation to the lower level gradually taking place.

If it is agreed that reduction in the level of the diastolic pressure is desirable, ganglion-blocking agents are the drugs of choice, in that they alone produce an immediate and definite fall in pressure. Maintenance of this effect is difficult to accomplish, owing to the development of tolerance to the drug, and is comparable to the regression following sympathectomy. It might be advisable to combine ganglion-blocking agents with other drugs which have different sites of action. A simple homologue of hexamethonium, pentolinium tartrate, has been found to be more useful in that it is more predictable in action, the duration of action is longer, and more stable control is obtained. It is probable that further work in the development of ganglion-blocking agents will result in the discovery of new compounds of greater value. Whatever the initiating mechanism of hypertension, the factor responsible for its maintenance is the arteriolar tonus, as has been shown by the response to sympathetic block. Treatment with ganglion-blocking agents must be regarded as symptomatic, in that no permanent alteration in the pressure level is achieved, and a rise always follows withdrawal of the drug. It is possible that at some future date advancement in knowledge of the synthesis and metabolism of cortical steroids may result in the production of compounds which will inhibit these, and will permit of a more fundamental control of hypertension. Alternatively, in that constriction of the arterioles is a function of noradrenaline, it is possible that means will be found to increase the activity of the enzyme iminase, which is responsible for the destruction of this pressor amine.

Summary

Although the prognosis in uncomplicated hypertension is usually good, elevation of the diastolic blood pressure is in many cases followed by symptoms and signs of heart failure, and when these develop the expectation of life is limited. General measures of treatment are rest, sedation, a salt-poor diet, and subsequent restriction of mental and physical activity. If these prove inadequate, and if the blood pressure is not labile, methonium compounds are indicated.

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A NEW CARBOHYDRATE-IRON HAEMATINIC FOR INTRAMUSCULAR USE

BY

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In recording the clinical trial of an unsuccessful intramuscular iron preparation (Goldberg and Hutchison, 1953) attention was drawn to the valuable, though limited, field of usefulness of intravenous iron therapy and to the wider applicability of intramuscular iron, could a suitable preparation be elaborated. The desiderata were that the preparation should be an effective haematinic freely absorbed from the tissues and non-irritating. Our recent experience with a new dextran-iron complex ("imferon") has convinced us that it is highly satisfactory for intramuscular use, and we present a preliminary account of our findings.

Methods and Materials

Venous blood was used for all haematological investigations, the anticoagulant being solid potassium-ammonium oxalate mixture (Heller and Paul, 1934). Haemoglobin was estimated by the method of Clegg and King (1942), using a Hilger photoelectric absorptiometer calibrated by crystalline haemin. 100% Hb was taken to be equivalent to 14.8 g. Hb per 100 ml. blood. The packed cell volume was determined by centrifuging the blood at 2,200 *g* for 30 minutes in sealed Hawksley haematocrit tubes.

The intramuscular iron preparation has been administered to two of us and to 15 patients suffering from iron-deficiency anaemia. These patients had haemoglobin values during the control period within the range 29–66% and were judged to be iron-deficient usually on three criteria—namely, low mean corpuscular haemoglobin concentration (M.C.H.C.), low serum iron, and absence of stainable iron in the sternal marrow (Hutchison, 1953). One patient, a woman with severe mitral stenosis, died shortly after treatment began; the cause of death was a massive cerebral embolus from the left auricle. Thus 14 patients have been followed up long enough for assessment of the haematinic effectiveness of the preparation (see Table). Of these 14 patients, 6 were known to be refractory to, and 2 had shown marked intolerance of, ferrous sulphate by mouth.

Before the commencement of treatment the test subjects were kept under observation for from seven to sixteen days, except in the case of one severely anaemic woman whose control period (three days) had of necessity to be short. Her own practitioner, however, vouched for a chronic anaemia of some months' duration in spite of treatment with both vitamin B_{12} and oral iron. During the control period in all cases two to five specimens of blood were examined to ensure that no significant fluctuation in the values was occurring and to provide a base-line by which to measure the effect of the preparation under trial.

Dosage.—The optimum dosage schedule is still under consideration, but 4 ml.—that is, 200 mg.—every other day into alternate buttocks has proved satisfactory; smaller amounts have also proved effective, but have the disadvantage of more frequent administration, and there are indications that response is more rapid when treatment begins with the larger doses. The patient's iron deficit was calculated approximately on the basis that 100 mg. Fe is equivalent to 4% Hb.

Details of Cases

Clinical Summary	Duration of Therapy (Days)	Total Iron Given (mg.)	% Hb		P.C.V. (%)		M.C.H.C.(%)	
			Before Therapy	After Therapy	Before Therapy	Therapy After	Before Therapy	After Therapy
1. F. 60. Achlorhydria. No haemorrhage	130	1,100	66	98	36·6	46·4	26·7	31·3
2. F. 39. No achlorhydria Slight menorrhagia ..	71	1,200	61	88	30·2	42·4	29·9	30·8
3. M. 61. Achlorhydria W.R.+. No haemorrhage	117	1,200	60	87	32·4	41·8	27·4	30·8
4. F. 66. Achlorhydria. No haemorrhage	97*	1,300	52	97	29·9	47·4	25·7	30·3
5. F. 42. Gastrectomy for ulcer in 1950. Menorrhagia	36	1,400	52	80	30·1	41·9	25·6	28·3
6. F. 65. Achlorhydria. No haemorrhage	50	1,400	46	89	28·9	44·6	23·5	29·5
7. F. 38. Menorrhagia ..	27	1,800	31	82·5	20·2	46·0	22·7	26·5
8. F. 43. Menorrhagia. Plummer–Vinson syndrome	47	1,600	37	83	22·2	39·3	24·6	31·2
9. F. 32. Plummer–Vinson syndrome	37	1,600	54	83	32·0	42·3	25·0	29·1
10. F. 62. Achlorhydria ..	55	2,000	31	72	20·5	37·9	22·4	28·1
11. F. 36. Achlorhydria. Menorrhagia	158*	1,800	44	93	26·0	45·0	25·1	30·6
12. F. 32. Achlorhydria. Menorrhagia	50	1,800	45	85	27·5	45·0	24·2	28·0
13. F. 28. Achlorhydria. Plummer–Vinson syndrome	50	2,000	29	76	19·0	44·0	22·6	25·6
14. F. 44. No achlorhydria	25	1,400	48	71	29·3	38·8	24·2	27·1

100% Hb = 14·8 g. Hb per 100 ml.

* In these two cases there was a considerable interval between the tabulated and the previous blood examinations, and the haemoglobin levels were probably reached much sooner than the figures indicate.

Results

Absence of Reactions Following Injection.—In no single instance was the injection followed by any general reaction, and no more than slight local tenderness was ever experienced even when a dose of 5 ml. was administered; in effect the preparation seemed bland and thus provided a striking contrast to preparations of intramuscular iron formerly tried. The serum iron in two instances was found to be sustained at a remarkably high level—for example, 2,860 µg.—for a period of days without any sign of toxic effect.

Haematological Response.—A significant rise in the serum iron content was demonstrable less than 18 hours after the initial injection. The reticulocytes were followed in some cases and showed a slight increase; a patient with 29% Hb initially showed 12% reticulocytes on the sixth day. In every patient a satisfactory rise in the haemoglobin took place. The speed with which this occurred varied, and factors which may be concerned are still under examination, but in general the rate of response was inversely proportionate to the initial haemoglobin level, and is probably to be interpreted as reflecting the degree of cellularity of the marrow. The slowest and most rapid responses are shown in Fig. 1. Over the whole series the average weekly rise in haemoglobin during the first month of treatment varied from 0.51 to 1.67 g. Hb per 100 ml. per week (3.5–11.3% Hb per week). The packed cell volume (P.C.V.) was more rapidly restored to the normal range than the Hb, the

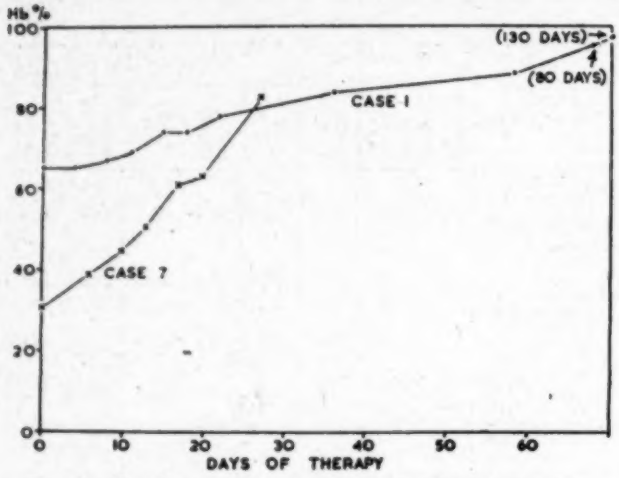

FIG. 1.—Showing variation in rate of haemoglobin response.

effect of this being to delay considerably restoration of the M.C.H.C. In Case 7 this is well illustrated. The Hb has reached a level 1.1 standard deviation short of the mean—that is, just within the normal range (Hendry, 1949), whereas the P.C.V. has exceeded the mean 2.6 S.D. and the M.C.H.C. is still 6.8 S.D. below the mean. In one case examination of the sternal marrow following treatment showed that stainable iron, absent before the starting of treatment, could now be demonstrated in the R.E. cells.

No attempt has been made to assess accurately or in detail the degree of utilization of the iron injected, but from the figures available this seems to be over 80% in some instances.

Discussion

This carbohydrate-iron preparation has been shown to be effective and non-toxic in the treatment of iron-deficiency anaemia. The rate of increase of haemoglobin varied in different cases, but, in general, was greater in young severely anaemic patients than in those beyond middle age with only moderate anaemia. In some patients clinical improvement became obvious within a week of the starting of treatment, while in others it was delayed for two to three weeks, but eventually all the patients in the series developed a vigorous sense of well-being which contrasted very strikingly with their previous chronic ill-health.

Compared with the intravenous iron preparations the new compound has the great advantages of easier administration and lower toxicity, while its therapeutic effect is similar. The only minor drawback was a tendency to staining of the skin in the area of the injection. This developed only in the first two patients treated, and was prevented in the others by injecting 1–2 ml. of air after the solution. The pigmentation appeared within 24 hours of the offending injection in both patients, and in the beginning was thought to be a bruise, but its true nature soon became apparent when, over the succeeding weeks, the colour changed to a slaty-grey, resembling the skin pigmentation of idiopathic haemochromatosis. Pigmentation was still obvious, although less intense, four months after the courses of treatment.

A small piece of pigmented skin was removed for histological examination from one of the patients three months afterwards; iron pigment was abundant in phagocytes in the corium, but melanin in the overlying epithelium was also increased, contributing to the pigmentation. Because of the possibility of skin pigmentation the site of injection should be the buttock and not the upper arm or thigh; this precaution is especially necessary in young females. None of our patients showed evidence of sensitization, either by a reaction during the course of injections or subsequently when the skin was tested with dextran. We have, however, heard of an instance in which urticaria developed immediately following an injection of this iron-dextran preparation (Dr. J. Wallace, personal communication), and the development of sensitivity in some instances is a possibility that should be borne in mind.

Serum total iron estimations proved that absorption took place rapidly from the muscles. The death from cerebral embolism of the cardiac patient provided an opportunity of studying the route of absorption, and at the dissection of the injection sites the application of the prussian-blue reagents to the tissues showed streaks of more intense iron staining in the fat which appeared to mark the course of lymphatics. The regional nodes were faintly brown, and histological examination subsequently (see Fig. 2) demonstrated large amounts of iron in the sinusoidal lining cells. Traces of iron could be seen in the lymph of the afferents outside the gland and also in lymphatics in the skin overlying the injection sites. It was clear from this that absorption was taking place via the lymphatics. When 200 mg. Fe was administered every other day sustained serum total iron levels of the order of 1,500 μg. were produced, but no appreciable loss of iron in the urine was detected.

The indications for the use of this new preparation are strictly limited and are the same as those for intravenous iron—that is, intolerance of or refractoriness to oral iron

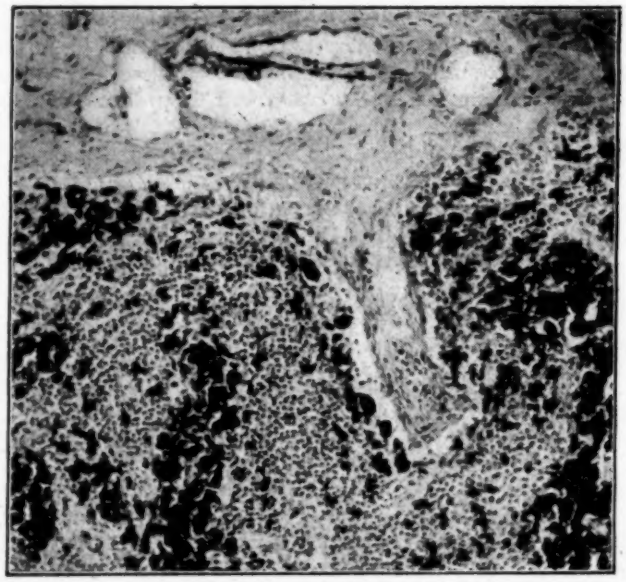

FIG. 2.—Lymph node draining injection site shows sinusoidal lining cells filled with iron. (Prussian-blue reaction. ×125.)

(Ramsey, 1950; Hawkins, Peeney, and Cooke, 1950), or circumstances such as pregnancy (Govan and Scott, 1949; Benstead and Theobald, 1952) or pre-operative preparation (Briscoe, 1952) in which a more rapid response than can be obtained with oral iron is desired. Since this carbohydrate-iron compound is much easier and safer to inject than saccharated iron oxide, parenteral iron therapy may become more popular, especially in general practice, for it ensures that the necessary quantity of iron is made available for haemoglobin synthesis and eliminates the uncertainties inherent in oral administration. Indeed, there is a possibility that it may become too popular. First, intramuscular iron might be prescribed too frequently for patients with iron deficiency who require only iron by mouth, but secondly, and more important, there might be a tendency to give it indiscriminately and in large doses to patients who do not have a deficiency of iron. The long-term effects of parenteral iron overdosage in humans are not yet fully understood, but, although the deposit of moderate amounts of surplus iron in the tissues does not in itself seem to be notably harmful, it is undesirable to administer this or any other parenteral remedy where it is not required. Accurate diagnosis and a proper trial of oral iron should therefore precede the use of intramuscular iron. The provision of an

effective, non-toxic, and easily administered intramuscular iron preparation should not be made an excuse for the indiscriminate use of parenteral iron therapy.

Summary

A preliminary account is given of the successful clinical trial, in 15 patients, of a newly elaborated proprietary dextran-iron haematinic ("imferon"). The agent proved non-irritating when given intramuscularly and was readily absorbed, giving serum iron levels of 600 μg. within eighteen hours; absorption via the lymphatics was demonstrated histologically. The complex proved an effective haematinic, giving average haemoglobin regeneration rates of between 3.5 and 11.3% Hb per week over the first four weeks of treatment.

We wish to thank the Medical Director, Research Department, Benger's Ltd., for supplies of imferon.

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ANAEMIA OF PREGNANCY TREATED WITH INTRAMUSCULAR IRON

BY

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AND

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The injection of iron intramuscularly as a therapeutic measure is no new procedure. As early as 1893 Stockman recognized the efficacy of this mode of administration, but, as he and subsequent authors (Barlow and Cunningham, 1911; Bullock and Peters, 1911; Witts, 1933; Heath, Strauss, and Castle, 1932) pointed out, the toxicity of the solutions employed was so great that only small quantities could be injected. Consequently, the rate of haemoglobin regeneration was actually less than that found with oral iron therapy. At the same time Heath *et al.* (1932) showed that the utilization of the injected iron for haemoglobin formation was nearly 100%. Fowler and Barer (1937) did not wholly agree with this. They stated that in all their cases the iron was retained, but in three out of four of their patients no improvement in haemoglobin level occurred. It was generally felt that until a less toxic preparation was available there was no real case for the intramuscular administration of iron.

The following is a report on the results obtained by the treatment of iron-deficiency anaemias of pregnancy with a new preparation "imferon" which can be given intramuscularly as well as intravenously.

Materials and Methods

Fifty pregnant women with iron-deficiency anaemia were treated with this preparation. All had haemoglobin values less than 10 g.%* In 14 the anaemia was mild—9 to 9.5 g.%; in 28 the haemoglobin lay between 8 and 8.9%, and in the remainder the anaemia was severe, haemoglobin being less than 8 g.%. All but one had a red-cell count over 3,000,000 per c.mm. This patient had a red count of 2,850,000 with a haemoglobin reading of 5.7 g.%. All were of microcytic hypochromic type with normoblastic marrows. Serum iron levels estimated by the method of Sven Dahl (1948) were uniformly low—from 10 to 65 γ per 100 ml., the average being 35 γ per 100 ml. Four of the patients were treated in hospital; the remainder were out-patients. Initially, two schemes of dosage were employed. Thirteen patients, including the four in hospital, were given daily injections equivalent to 100 mg. of elemental iron. Others received larger doses, representing 250 mg. of elemental iron, twice weekly. Subsequently all patients were treated with the larger dose. This preparation of iron is much more concentrated than the intravenous forms involving the use of the saccharated oxide. Each millilitre contains 50 mg. of elemental iron.

Daily estimations of haemoglobin, haematocrit values, and reticulocytes were made on those patients receiving daily injections. Similar estimations were made at regular intervals on other patients. Each week a complete investigation was made on all patients. Serial estimations of serum iron were made in selected cases.

*68% on the scale of 14.8 g. ≡ 100%.

Results

Daily haemoglobin and haematocrit readings, carried out on those patients receiving the smaller dose, revealed a characteristic pattern of changes somewhat similar to that found in patients treated with intravenous saccharated iron. The haemoglobin rose slightly during the first 24–48 hours. Thereafter a fall occurred, a minimum value being reached by the fourth day of therapy. Subsequently there was a rapid improvement. These sudden initial changes in haemoglobin were probably due in part to variations in blood volume. Curiously, however, the haematocrit reading increased from the beginning and there was a similar increase in mean cell volume. It is likely that these increases were caused by an outpouring of normocytes from the marrow, and this might tend to mask blood-volume changes.

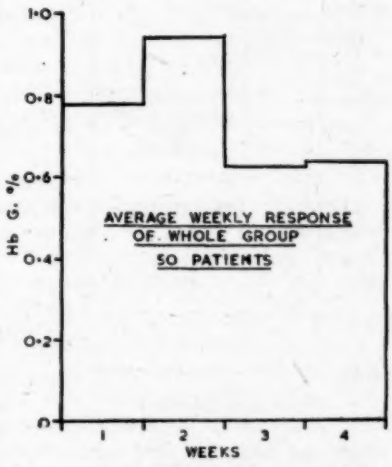

FIG. 1.—Average weekly haemoglobin increments of whole group.

The average haemoglobin increments during the first three weeks following treatment are shown in Fig. 1. During the first week the average increase was 0.77 g.%. The average increment for the whole group during the second week was 0.94 g.%. By the third week many of the cases were almost normal, and the percentage increase for the group was only 0.62 g.%. Study of the cases, however, indicated that, as with all forms of iron therapy during pregnancy, two main types of response were shown. Adopting an arbitrary response of 0.5 g. as a significant figure, it could be shown that, during the first week of therapy, in the greater proportion of patients (42) the haemoglobin increased by 1.1 g. In the remaining eight patients the increase during this period amounted to only 0.22 g. During subsequent weeks the response of both groups was similar. Haemoglobin increments of the two groups are shown in Figs. 2 and 3.

Reticulocytes, from an initial value of less than 1%, showed a significant rise by the fourth day and reached a maximum on the seventh. Levels were higher in the more severe cases, and the greatest increase, 6.8%, was found in a young patient whose initial haemoglobin was 6.2%. The average for the whole group was 3.8%.

Utilization for haemoglobin production was extremely good. An average haemoglobin increase of 0.3 g. was recorded for every 100 mg. of elemental iron injected. The smallest increase, 0.21 g., occurred in a patient with a twin pregnancy, and the highest, 0.66 g., in a case of early pregnancy. These findings, however, will have to be confirmed over a larger series, since the response will naturally vary with the weight of the patient and her blood volume.

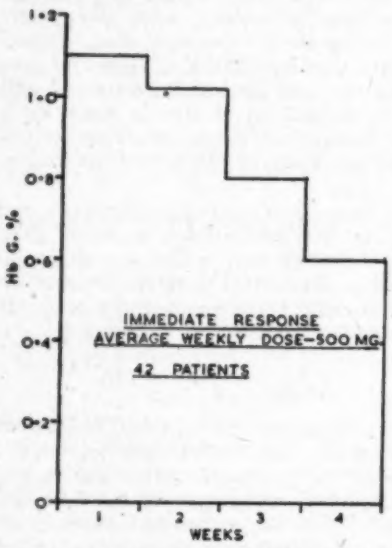

FIG. 2.—Haemoglobin increments in patients showing rapid response to treatment.

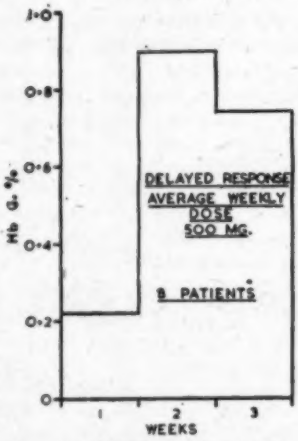

FIG. 3.—Haemoglobin increments in patients in whom response is delayed.

Serum Iron

Serial estimations of serum iron were made in nine patients. Five received daily injections of 2 ml. of the preparation (≡ 100 mg. of elemental iron), and the serum iron was estimated at the same time each morning before the injection was given. Twenty-four hours after the first dose the readings, previously low, were remarkably high, 335 to 820 γ per 100 ml.; and the levels mounted steadily with each injection. In the more severe cases the levels were not so high, suggesting possibly that the utilization was more rapid. The number of cases is small, however, and no doubt other factors, such as marrow activity, play a part.

With larger doses the serum iron increases were less regular, but extremely high levels were often found. In two patients given 5 ml. daily for four and five days respectively, the serum iron readings 24 hours after the last injection were 2.26 mg. and 1.87 mg. per 100 ml.

Serial readings following a single intramuscular injection equivalent to 250 mg. of elemental iron showed a steadily rising curve during the subsequent 36 hours. This preparation can be given equally well intravenously. Estimations following a single intravenous injection of 250 mg. of elemental iron showed very high readings immediately, with a fall to a level at 48 hours almost the same as that recorded with the intramuscular route (Fig. 4). Successive intravenous injections produced further augmentation of the serum iron level, and readings as high as 7.5 mg. per 100 ml. have been found.

General

The most remarkable features of this new preparation are the facility with which it can be administered, and the absence of reactions, either local or general, provided care is taken to give the injection properly. It must be made deep into the muscle of the upper and outer quadrant of the buttock, using a large-size needle. If it is injected into the superficial fat a persistent brown staining of the subcutaneous tissue will result and there will be a lack of absorption. Apart from a slight initial stiffness common to all intramuscular inoculations, no untoward effect has been observed. Similarly, despite the very high serum iron levels, no general reaction which could be clearly attributed to the preparation was encountered. One patient developed a maculopapular rash on the extensor surfaces of both arms. This patient, however, had previously suffered from dermatitis. After the rash disappeared further treatment failed to provoke any reaction, and it is considered that the skin rash was merely coincidental. Since large amounts of iron may be given in a single dose the number of injections can be reduced. It is often found that patients treated with oral iron fail to respond until they are admitted to hospital. This may be due to some defect of absorption corrected by rest, or merely because the patient fails to take the medicine as prescribed. With this simply administered preparation the need for admission to hospital is eliminated.

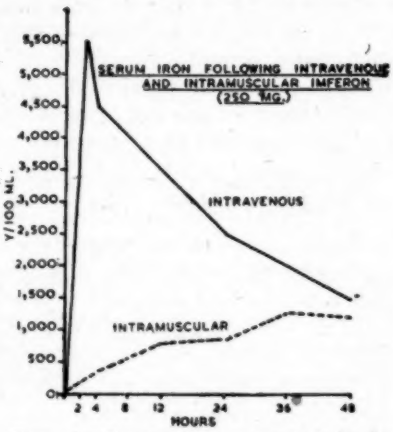

FIG. 4.—Serum iron curves following intramuscular and intravenous injections of 250 mg. of "imferon."

Commentary

This preparation naturally invites comparison with the widely used saccharated oxide of iron, which can only be administered intravenously (Govan and Scott, 1949; Scott and Govan, 1951). As already stated, the ease with which the injections may be made and the absence of reactions, despite the relatively high doses of iron, are among the most important characteristics of this preparation. The response is equal to that obtained with intravenous saccharated oxide of iron. In a previous series of 91 patients treated with the intravenous preparation (Scott and Govan, 1951) the average haemoglobin increments during the first three weeks of treatment were 1.0 g., 0.9 g., and 0.4 g. per 100 ml. The present results of 0.77 g., 0.94 g., and 0.62 g. per 100 ml. are equally good. Utilization of the iron for haemoglobin production is exactly the same for the two compounds, both resulting in an increase of 0.3 g. of haemoglobin per 100 mg. of elemental iron. As with the intravenous preparation, significant improvement may be delayed for a week. This is characteristic of many cases of simple anaemia of pregnancy no matter how or in what form the iron is administered. With oral iron preparations improvement may be delayed for as long as one month.

With the higher concentration of elemental iron (50 mg. per ml.), as compared with intravenous saccharated oxide of iron (20 mg. per ml.), a higher dosage schedule may be instituted, thus reducing the number of injections.

The extremely high serum iron readings, combined with the absence of reactions, is interesting. Similarly high readings were obtained with saccharated oxide of iron only when very large quantities, up to 1 g., were injected, and this was associated with a greatly increased incidence of reactions. Obviously the serum iron readings *per se* have no direct relationship to the onset of reaction. In the present series, levels well above the plasma iron binding

power (Klopper, 1951) were obtained without having any undue effect. It would appear that the nature of the iron compound and its stability are more important than the amount given. Our results would tend to support the view of Nissim (1954) that reactions following use of saccharated oxide of iron are due to precipitation of an inherently unstable compound.

Summary

The results of treatment with a new intramuscular preparation of iron in 50 cases of anaemia of pregnancy are recorded. All patients were in the antenatal period.

In 14 patients the condition was of mild degree, in 28 it was moderate, and in 8 it was severe. All responded satisfactorily. An average weekly dose equivalent to 500 mg. of elemental iron produced an increase of slightly more than 1 g.—that is, 6% on the Haldane scale. Utilization of the iron was good, the haemoglobin increasing on the average by 0.3 g. for every 100 mg. of elemental iron injected. These results are almost identical with those obtained by the use of intravenous saccharated oxide of iron. As with all forms of iron therapy, response to treatment was sometimes delayed, but by the second week of treatment all patients showed similar haemoglobin increases.

The preparation contains 5% elemental iron compared with 2% in those utilizing the saccharated oxide of iron. With this concentration the number of injections may be reduced considerably. Many cases of mild anaemia require only two 5-ml. ampoules. Very high serum iron readings result from the injection of this highly concentrated solution, but no reactions, either local or general, have so far been encountered.

We would like to thank Benger's Ltd. for generous supplies of imferon for clinical trial.

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The General Board of Cambridge University, in a Notice in the *Reporter* of November 17, state that they consider that former University teaching officers should not be employed to give regular courses of instruction unless it is clear that by so doing they will not block the way to promotion for others. With certain exceptions, continues the Notice, the Board "will therefore not approve the estimates of a Faculty or Department which desires to employ a former University teaching officer unless they have received an assurance that other teachers will not thereby be precluded from appointment to office or from having their fitness for promotion tested. The Board will be prepared to consider the approval of estimates which include provision for the payment at the normal rates of a former University teaching officer to give a regular course of instruction when a University teaching officer falls ill or is away on leave and is therefore unable to carry out his regular teaching duties, and it is found difficult to replace his teaching work without seriously disorganizing the work of other members of the staff. They will also consider the approval of estimates which include provisions for the payment at the normal rates of former University teaching officers to give specialized courses to meet particular needs not forming part of the instruction for a Tripos or Part of a Tripos."

A PREVENTIVE APPROACH TO COMMON DISEASES OF THE LUNG*

BY

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Preventive medicine, together with a rising standard of living and recent therapeutic developments, has led to a marked rise in the expectation of life of children born into our community. Since 1841 this has amounted to 27½ years—but there has been no equivalent increase for those aged 60. In fact, during the same 110 years the expectation of life at this age has risen only one year for men and four years for women (Logan, 1953). The great killing diseases at this time of life are those affecting the cardiovascular system and the lungs. A preventive approach to these should pay handsome dividends. However, despite much research, the problems of cardiovascular disease remain unsolved. The major lung diseases—bronchitis, pneumonia, cancer, and tuberculosis—do not present such baffling problems. Sufficient is known of their aetiology now to make prevention possible in a community alive to the simple facts governing these lesions of the chest. The deaths, mainly in the older age groups, amount probably to 100,000 per year, but death is preceded by months and often years of invalidism in many cases. This is certainly true of the too common condition of bronchitis. In 1950 it was responsible for the loss of 16,500,000 working days amongst our insured population. A high incidence of chronic chest disease is accepted by us—but a careful study will show that most of this is avoidable. This study is essential in a community where healthy ageing is one of the most pressing problems of society.

The industrial revolution brought great wealth to our country, but resulted in a growth of industrial cities where a spectacular rise in morbidity and mortality took place. Between 1831 and 1841 the crude death rate per thousand in Birmingham, Leeds, Bristol, Manchester, and Liverpool rose from 20.6 to 30.8 (Griffith, 1926). Great efforts were made subsequently to deal with intestinal diseases which were responsible for the most spectacular part of the rise. Cholera, typhoid, and dysentery were gradually controlled. This was achieved, after many bitter struggles, by the supply of clean water and the effective clearing of sewage.

Respiratory diseases remained, but the need for attention to the grossly polluted air was apparent to the great reformers Chadwick and Simon—in fact, Chadwick projected a "pure air company" to suck down pure air from specially constructed towers into the dwellings and workshops of city populations. Coal was abundant and cheap. Industrial cities had grown up, consisting of houses, surrounding factories, foundries, and mines. "The towns sprang up at a nightmare rate and of a nightmare character. Fastest of all grew the cotton towns; the iron towns, the woollen towns, the pottery towns followed hardly less swiftly, while all about the coalfields gaunt mining villages grew side by side with fiery waste heaps in the very shadow of the pitheads, often enough in the pit yards themselves." (Sharp, 1950.) Here the air was and still is heavy with smoke, fumes, oxides of sulphur, and other products of combustion. The urge for hygienic reform spent itself before clean

*Based on a lecture given to the Salford Division of the British Medical Association, May, 1954.

air was obtained. Later the economic depressions left many smokeless chimneys. Now in the industrial areas chimneys belching smoke are almost welcomed by those who live beneath their shadow. They are signals of continuing employment.

It is time, however, that the air we breathe is recognized to be as important as the water we drink. We still treat the air over our large towns as a sewer; into it chimneys belch thousands of tons of harmful grits, solids, and gases each year. Thus we have failed to learn the lesson of the Thames. Last century London poured its sewage into this river and from it, at many levels, water companies drew their supplies. Because of this, typhoid, cholera, and dysentery knew no bounds. Today the same situation faces us in every industrial area in respect of lung disease. When the air we breathe is regarded as seriously as the water we drink, then can we hope to have and retain healthy lungs.

Atmospheric Pollution

Two aspects of atmospheric pollution are very important: general atmospheric pollution, and dust and fumes at work.

Atmospheric pollution results mainly from unburnt carbon and other solids of coal combustion, together with sulphur gases, SO_2 and SO_3. In appropriate weather conditions these form aerosols which give rise to disastrous consequences. The great fog of December, 1952, killed 4,000 people in fourteen days in London. Some have asserted that it killed somewhat prematurely those who would have died within a short time. There is no justification for so dismissing the effects of the most lethal fog recorded in world history. It is not widely realized, however, that this "smog" was the starting-point of recurrent bronchitis in many thousands of Londoners. These effects were dramatically demonstrated in the country's best cattle, then on show at Earl's Court. Their healthy lungs were overwhelmed by our polluted air. Prize cattle on the ground floor developed acute suffocative symptoms. Five died, some had to be slaughtered, and others were saved only by emergency measures. Post-mortem examinations showed acute bronchiolitis, emphysema, and right heart failure. No better experiment could have been devised, and Londoners were rightly alarmed by this catastrophe. The London Local Medical Committee did well to advise the wearing of masks in any similar fog. Two years later no official advice, guidance, or preventive ideas have come from the Ministry of Health.

Details of this smog are interesting and important. Its centre of density was in Westminster and the central area of London. Since 1931, 1,200,000 people have left the centre of the city—while those remaining live more in flats where gas and electricity rather than coal-fires supply heat. Meanwhile, the great coal-consuming plants—electricity, gas, and transport—have increased disproportionately. Since 1921 there has been an increase of 400% in the coal burned to produce electricity. Our own hospital has four generating stations within a short distance of it. These consume over 500,000 tons of coal annually. No attempt is made to extract the sulphur gases from their effluents, although much less visible smoke is produced than when the same amount of coal is burnt domestically. Future generations will marvel that the nation not only permits this, but that, despite our experiences in 1952, bigger generating stations are being erected within London's built-up areas. Meanwhile attempts are made to deflect attention from these offending consumers to the domestic grate; only 18% of the nation's coal is burned in the home—it is burned inefficiently, but it does not produce the major pollution with oxides of sulphur. It is regrettable, too, that hospital chimneys offend both local by-laws and sanitary sense by pouring black smoke into the atmosphere for hours on end. Just as during last century we failed to appreciate the part played by infected water, so now we neglect the effect of polluted and infected air.

Dust and Fumes at Work

It is by altering conditions at work that we can hope to get the greatest improvement in our morbidity and mortality rates in chronic chest illness. Our industrialization took place much earlier than in many other countries: coal as a source of power was plentiful throughout our island; iron, clay, and other raw materials of basic industry were close at hand. We led the world in many developments at a time when industrial hygiene was almost unknown. Many of the processes remain with us, and hygienic measures have not caught up with those associated with more recently developed industry. Consequently we find such processes as mining, pottery, foundry work, cotton-spinning, quarrying, etc., taking a huge and avoidable toll of our people. Much investigation has been undertaken to show that these and allied industrial processes produce specific effects in the lungs. This undoubtedly does happen in many cases. However, it is essential to emphasize that the first effect of inhaling dust or toxic fumes is to produce cough. Cough is the warning signal that the air we are breathing is contaminated. This cough, of course, may not start at the moment of inhalation, but may be present after some hours, especially in the morning following the previous day's exposure. Satisfactory air conditions at work will have been established when it can be shown that no cough is produced after a minimum exposure of five years. Meanwhile, all of us seeing patients working under adverse conditions should look for the early evidence of continuing chest disease.

The Mines

The attitude suggested above is essential when considering one of our most valuable workers—the miner. The full extent of chest trouble is unknown in these workers, and there seems an unnecessary reluctance to discover the truth. No adequate preventive action will be taken until this happens. The *x*-ray survey of the mining valley—the Rhondda Fach—showed that approximately 50% of all miners and ex-miners have radiological evidence of dust disease. This indicates fairly gross structural damage which is irreversible and much of which will progress, even though no further mining is undertaken. However, this takes no account of chest symptoms. These are known to the practitioners responsible for the day-to-day treatment. Crude death rates from bronchitis for hewers and getters and their wives compared with farmers and their wives reveal the following figures:

Hewers and getters	..	crude death rate	622 per million
Hewers and getters' wives		,, ,, ,,	144 ,, ,,
Farmers		,, ,, ,,	184 ,, ,,
Farmers' wives		,, ,, ,,	77 ,, ,,

The sex difference, judged by crude death rates, is nearly twice as great in colliers as in farmers, suggesting occupational factors of importance. Of course, figures for pneumoconiosis are not included in the case of colliers, and in none of these four groups are all the cases of chronic bronchitis included, for cor pulmonale and pneumonia are given separately in the Registrar-General's report.

An inquiry into the certified causes of death in one mining practice showed that of 87 miners and ex-miners dying since 1946, 42 had died of chronic chest disease; of these only two had been certified as having pneumoconiosis. These isolated figures suggest a rate of 100% above the average for the general population. Here is a great problem for research and subsequently for remedial measures in the mines. Our aim should be to ensure such a dust-free air that the miner coughs no more than other men working in good conditions.

The combination of dust, particularly silica, with tuberculosis is probably responsible for the most serious chest complaint—progressive massive fibrosis. This is known to be common in South Wales, and is probably commoner than is suspected in other mining areas. It is progressive and quite untreatable. Its prevention is urgent. Tuber-

culosis amongst the miners and their families should be given increasing attention. An annual *x*-ray examination of all in these families over 15 years of age for the next five years and the immediate treatment of any infectious case would probably do much to eliminate this common and fatal condition.

Other Industrial Hazards

Space does not permit a detailed analysis of other industrial problems; but wherever there is harmful dust, so irreversible lung changes occur. We should attempt to see that steps are taken in each industry to detect an increased incidence of chest symptoms. In the past compensation has been the workman's only solace for the ills that work has inflicted upon him. Compensation is rarely paid for avoidable chest disease until irrecoverable damage has been done. Future activity—while retaining compensation as the last line of defence—should aim at pure air and healthy lungs. Practitioners in industrial areas will know what benefits would result to their patients if this could be achieved. Much effort, often uncoordinated, has gone into the improvement of working conditions, but many men with serious chest disease are still allowed to drift from one unsuitable occupation to another. Two instances seen recently will illustrate this point:

An ex-miner aged 56 with considerable pneumoconiosis—not certified—sought work in London. He eventually settled in a local foundry, cleaning castings coated with sand. He died of congestive heart failure secondary to chronic chest disease five years after taking up such work.

A miner aged 45 with progressive massive fibrosis came to London and obtained work without medical examination in a factory where cases of bagassosis have arisen.

A nation-wide occupational health service is surely needed to establish standards of healthy environment at work, to make certain these are implemented, and meanwhile to see that the partially disabled are not further handicapped by unsuitable working conditions. We pay much lip-service to "preventive medicine." Are we not missing in our own day and in our own country an opportunity which common sense would say is obvious? The price of neglecting to take reasonable preventive measures has to be paid in terms of damaged health, impaired efficiency, time off work, sickness benefit, and medical treatment. Prevention is not only good medicine—it is sound economics.

These factors, together with infections, overcrowding, and a poor standard of living for many town dwellers, have combined to give us a most unenviable reputation for chronic chest disease. Figures quoted by Fry (1954) suggest that we have a much higher incidence of bronchitis than practically any other country where morbidity and mortality figures are kept. As a nation we are now characterized by a chronic and ubiquitous cough, and we attempt to minimize this by laughing it off. The phrase, "my smoker's cough," frequently hides an anxiety and a disease that ought to be investigated. Cough is a serious symptom—it warns of excessive irritation of the bronchi. Thus it resembles vomiting, but we treat it much more lightly. Until the community and the profession regard coughing as seriously as vomiting, so long will much chest disease remain uninvestigated; so long, too, will avoidable vitiated air be breathed and tolerated.

Smoking

Smoking presents us with one of the greatest social problems of our times. The habit is so widespread and the ill-effects are insidious and often long delayed. The pleasurable results are emphasized by direct and indirect advertisement throughout the whole structure of our society. An attempt at dispassionate consideration makes one wonder whether many would smoke if the untoward effects of the initial cigarettes, and the fatal effects of the combined total, were not obliterated in the public mind by ubiquitous propaganda. Whatever the explanation of the country's heavy smoking, the effects, in terms of cough, bronchitis, emphysema, and cancer of the bronchus, are becoming very obvious. Few people who smoke 15 or more cigarettes daily for 20 years fail to develop a morning cough. This grows worse as the years pass. Infection and other factors mentioned have an added effect. Many who are more sensitive to the irritant effects of smoking will develop a cough and a tendency to bronchial spasm when consuming fewer than 15 daily. Our approach to this problem is clouded by our own reaction to the cigarette. Until recently, tobacco consumption by the profession has equalled that of the general public. Many of us are very heavy smokers; our reactions are thus often emotionally determined. However, the crude ill effects of this habit are now so widespread that we have a duty to attempt a scientific approach to the problem. For patient and doctor, a complete abstinence from cigarettes for three months will usually demonstrate a relationship to coughing, and further scientific proof will not be needed.

Teeth and Sinus Infection

So many patients with severe bronchitis have gross dental infection that it is impossible to dissociate the two conditions. Considerable improvement often follows the removal of this local obvious source of irritation. Much more rarely does chronic sinus infection appear to play an important part. However, where other factors do not seem important, and where *x*-ray examination yields evidence of pathological change in the sinuses, treatment should be directed to these.

Bronchitis

This is one of our most difficult problems and one to which consultants in hospital practice have given too little attention until recently. In fact, chronic bronchitis has not yet received an adequate definition despite its frequency. It may be defined as a cough causing increasing illness and loss of working capacity, unassociated with any specific abnormality in lung structure and usually unassociated with any specific infecting organism. All too frequently we in hospital have been content both to assure the patient with bronchitis and the practitioner that there is no organic disease and to assume that our responsibility ends there. This attitude can no longer suffice; for, as the more specific acute infections have yielded to therapy, so the extent of bronchitis becomes manifest. It causes 30,000 deaths a year and the loss of 16,500,000 working days. Meanwhile, 20,000 die annually from pneumonia, and many of these have had chronic chest disease. Death from pneumonia, affecting previously healthy lungs, is a rare phenomenon to-day.

Bronchitis is a cumulative disease. Each set-back—such as a severe fog, infection, or excessive exposure to dust—may lead to increased lung damage and a diminished expectation of life. Until a certain stage is reached it is reversible and good health can be restored. Steps must be taken sufficiently early to discover the factors which irritated the bronchi and maintained the cough. Careful history-taking will often reveal a fascinating and formidable group of factors. The important ones can be summarized as follows: (1) Social factors: (*a*) place of residence: bronchitis is five times as common in some large towns as in the country; (*b*) social class: it is five times as common among unskilled labourers as among professional men. (2) Infections: (*a*) in early life, and (*b*) at 40–50 years of age. (3) Occupational factors. (4) Smoking. (5) Infected teeth and sinuses. (6) Allergy. (7) Gassing in 1914–18 war.

The overcrowded home in poor quarters of the industrial town has been, and is, responsible for much bronchitis in infancy and childhood. This follows particularly the specific infectious fevers. Recurrent bouts of upper respiratory infection pass around the household and thus an almost continuous cycle is maintained. Associated with this home environment, the overcrowded schoolrooms offer excellent opportunities for the constant exchange of

organisms. A little later in life, travel in the rush hours in most cities is a fruitful source of trouble. The smoke-laden atmosphere of bus, tube, or train is likely to irritate and then to infect susceptible bronchi.

Often a febrile illness with respiratory symptoms beginning at 40 years of age or over will initiate a train of events leading to the establishment of chronic bronchitis. Virus infections of an influenzal nature are prone to do this. It is essential that both in the young and in the middle-aged we should attempt to ensure a complete recovery from these illnesses.

The occupational history is often most revealing—and it is very desirable that all of us should have a wide understanding of the working conditions of our patients. Time spent as a student or after qualification in factory, foundry, or mine will enable us to understand why many patients cough. It will make us more insistent upon complete recovery from cough before work is resumed. This is very important in men working in heavy industry, for they are extremely liable to develop emphysema and its most fatal complication, cor pulmonale, as shown by Flint (1954).

The reversible aspect of bronchitis has been stressed. This phase passes as emphysema develops, and it is essential that we should bring all preventive measures to bear on this too common complication. Emphysema is rarely seen in the absence of chronic cough—or, again, in the absence of smoking. Once established to a degree that gives rise to symptoms and unequivocal physical signs, deterioration and death follow after years of invalidism and suffering. Abbott *et al.* (1953), investigating the aetiology of severe emphysema, found smoking more than 20 cigarettes daily to be the common factor. No improvement in symptoms was obtained while this continued.

Effective action at a stage where it can be beneficial lies with the practitioner, for the insidious development of chronic cough and subsequent lung damage can be detected only by those in close and continued contact with the patient. The wife's point of view is often worth attention—for the bronchitic male will often minimize his symptoms because he knows that his own habits contribute to them.

Lung Cancer

The spectacular rise in deaths from lung cancer in this and all other countries where cigarette-smoking has been common for 25 years or more is now established. The relationship between this habit and the incidence of at least 80% of these cancers is no longer doubted by scientific observers. The high rate of mortality is still not appreciated by many of the profession who are not specializing in chest disease. These deaths now exceed the combined total of those due to road accidents and to pulmonary tuberculosis.

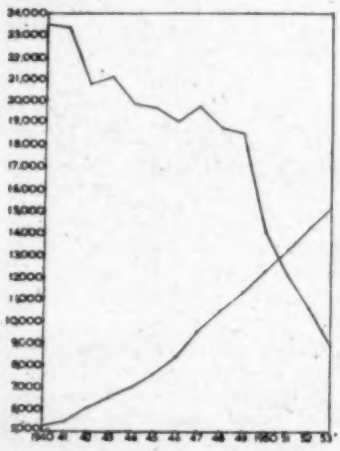

FIG. 1.—Deaths from pulmonary tuberculosis (falling curve) contrasted with those from cancer of lung (rising curve).

Fig. 1 shows the way in which this continued rise in mortality has now more than compensated for the spectacular fall in the tuberculosis curve. All available evidence suggests that, unless the community rids itself of its cigarette addiction, this steeply rising curve will continue until at least 1970, when over 25,000 people will die annually in England and Wales. This rise is avoidable. We in the profession can be of the greatest assistance, both by example and precept. There is no magic in a cigarette which can compensate for the harm it does. Doll and Bradford Hill (1954) show that we doctors are dying in the same way as our patients. Surely intelligent self-preservation, if no other motive, should ensure that we take part in a great campaign of preventive medicine.

Meanwhile, the probability of carcinoma of the lung in any patient over 45 years of age who has smoked for 20 years or more should be always before us. If treatment is to be of great assistance, earlier diagnosis is essential. Many of the growths start silently in the outer part of the lung. There is no reason why symptoms other than those due to smoking should be manifest until a late stage. Consequently, until some more delicate indicator of cancer is available, there is much to commend annual chest *x*-ray examination of all who continue to run this risk and who are 45 years of age and older. In fact, Boucot and Sokoloff (1954) advocated six-monthly checks. The slow symptomless growth is illustrated by Figs. 2 and 3 taken from a patient in whom hypertension, generalized bronchitis, and polycythaemia precluded the possibility of operation. These show that for twelve months the growth remained operable, while no symptoms referable to the lesion existed. The insistence on frequent radiological examination will also bring home to the population and the Government the need for preventive action. The scope of beneficial activity by the general practitioner was never wider than in this situation.

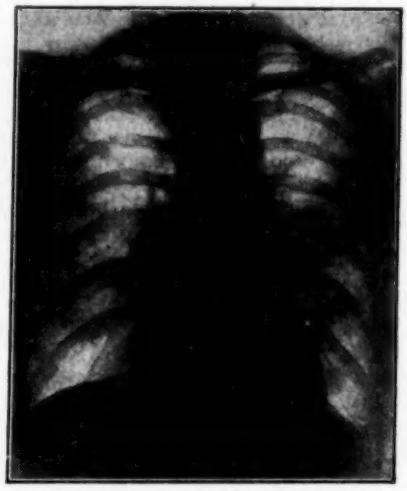

FIG. 2.—Radiograph taken on March 31, 1953, showing peripheral carcinoma at apex of left lower lobe.

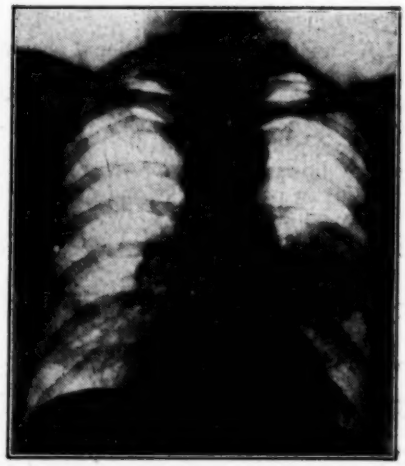

FIG. 3.—Radiograph in same patient as Fig. 2 taken twelve months later showing growth still apparently operable.

Tuberculosis

Modern therapy, modern diagnostic facilities, and known methods of prevention are altering the whole aspect of tuberculosis. There is a tendency in some quarters to play down the need for continued vigilance and activity in eradicating this disease. The Home Office and other departments have refused to take steps to ensure that people coming from abroad to work amongst us are free from active and infectious disease. This is contrary to the policy of practically every other English-speaking nation. More important, it is contrary to common sense, for it fails to bring home to us all that this is an infectious and therefore a preventable disease. The possible application of B.C.G. vaccination to tuberculin-negative immigrants from Ireland and elsewhere should be explored, as suggested by Hess and Macdonald

(1954). We must aim to give what protection we can to those who are especially susceptible.

The practitioner is in a strong position as regards early diagnosis. Case finding is highest in those people referred for *x*-ray examination by practitioners. There is no effective substitute for a practitioner who is quick to detect and act upon early suggestive symptoms or signs. As a corollary it should everywhere be an easy matter for a doctor to have his patient *x*-rayed. Where facilities are still lacking, they should be pressed for insistently until made available; miniature films are inexpensive, are quite efficient, and are useful in this connexion.

Hospital and sanatorium treatment is now much more available in most parts of the country, but some areas lag behind. Long waits for surgery—up to two to six months—are still existent; these, apart from anything else, result in wasteful blockage of beds.

Regional hospital boards and hospital management committees are sensitive to criticism on this matter. If there is delay in effective treatment, pressure by a practitioner will do much to obviate it.

The policy of vaccinating school-leavers with B.C.G. remains in a far too nebulous state. No clear lead has been given. The evidence available should be sifted as soon as possible with a view to establishing a national policy. The full possibilities regarding hostels for continued segregation and sheltered workshops require further study, but this should be undertaken with a view to promoting a suitable scheme of action and not lead to further delay. Evidence is still awaited regarding the most appropriate regime of chemotherapy for the long-term sputum-positive patient, and at what intervals it should be applied.

Summary

It can be asserted that chest disease presents us with a challenge. Much of it is preventable—it is not being prevented. Our community and our profession are dying needlessly. Clean and uninfected air in town and workplace is essential—it can be obtained. Cigarette-smoking has been shown to be more dangerous to health than any other national habit. Unless the irritant and carcinogenic effects can be eliminated, further manufacture and sale should be seriously questioned. No consideration of tax collection should blind us to the need for action.

Last century saw great progress in eradicating intestinal disease. More spectacular progress can now be made in ridding us of diseases of the chest. This challenge is a personal and a national one. Economically, action is essential—humanely, it is imperative.

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Health education was considered mainly from the nursing point of view by a group of doctors and senior nursing personnel at the 1954 Summer School arranged by the Central Council for Health Education at Reichel Hall, Bangor, North Wales. The group rejected the suggestion that specially trained health educators were necessary in hospitals. After the medical staff, the ward sister was the key person in instructing patients and their relatives. But if she were to have time to do this properly it might be necessary to lighten some of her other duties.

INCREASED PLASMA BILIRUBIN IN NEWBORN INFANTS IN RELATION TO BIRTH WEIGHT

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Some degree of jaundice is often shown by newborn babies in whom there is no evidence of haemolytic disease. The extent and duration of jaundice are rather variable (Davidson *et al.*, 1941), but are thought to be more marked among premature infants (Hsia *et al.*, 1953). The condition is generally regarded as an innocuous one, as is implied by the customary description—"physiological jaundice." However, a more serious view is suggested by recent reports (Aidin *et al.*, 1950; Claireaux *et al.*, 1953), which show that prematurity and jaundice may be followed by pigmentation of the brain and death of the infant. This association had led us to re-examine the relation between birth weight and the incidence, degree, and duration of the increased bile-pigment content of the plasma of newborn babies. The nature of the plasma pigment has also been determined, since there is evidence that bilirubin is damaging to the brain.

Methods

The basis of the survey was a series of plasma bile pigment estimations, at approximately daily intervals, on a group of "normal" newborn babies which were selected to provide a wide range of birth weights. In order to determine the highest plasma pigment concentration reached in each baby the study was continued until the amount of bile pigment in the plasma had dropped markedly from the previous day's figure, or had dropped appreciably on two consecutive days.

Birth Weight.—This was drawn from the hospital case records.

Selection of Patients.—The one criterion for including a baby in the survey was its birth weight. During the period of this investigation all babies in certain wards, up to a maximum of nine babies in each weight group, were studied, excepting those babies that were known to have haemolytic disease or some other pathological feature. The plasma pigments of some very small babies were not determined during the first day or two because of their clinical condition. Additional babies, to whom attention was drawn because they were jaundiced or deeply jaundiced, were studied with respect to the type of serum pigment, but are not included in the series.

Bile Pigment Estimations.—Heel-prick blood was collected with heparin or oxalate, and 0.05 to 0.2 ml. of plasma was used for quantitative estimation by van den Bergh's diazo technique (King, 1951). For the most part estimations were made daily, though there were occasional intervals of 48 hours.

*Working on a grant from the Medical Research Council.

Identification of Pigments.—Extracts of plasma pigments were prepared and examined chromatographically (Cole and Lathe, 1953) to distinguish bilirubin, which is indirect-reacting, from the other bile pigments which react directly in the van den Bergh test.

Results

Amounts of Bile Pigment.—The study included 49 babies ranging from 2.75 to 10.24 lb. (1.2 to 4.6 kg.) birth weight. Of these, 19 were "premature" infants—that is, they weighed 5.5 lb. (2.5 kg.) or less at birth. For analysis the premature and normal-weight infants were divided at pound intervals into three and five groups, respectively. The changes in plasma bile pigment were plotted for each baby and the maximum height and the day on which this occurred were noted. The maximum height of plasma bile pigment of the babies in each group is plotted as an average, and standard deviation, in Fig. 1. The day on which this peak occurred is presented in a similar way in Fig. 2. It would have been desirable to plot average curves of daily bile pigment concentrations for the babies of each weight group, but as the same number of samples were not taken from each baby this method was not satisfactory. As an alternative, individual graphs of five "typical" babies, varying in weight from 3.8 to 9 lb. (1.7 to 4.1 kg.) are given as examples in Fig. 3.

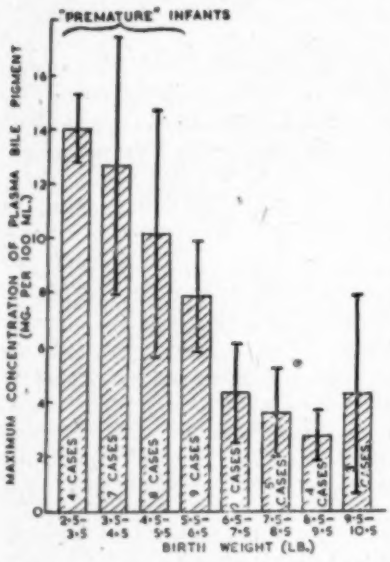

FIG. 1.—Relation between the birth weight of infants and the maximum concentration of plasma bile pigment which occurs during the neonatal period. The average for each weight group is shown as a column, and the limits of one standard deviation are shown as a vertical line.

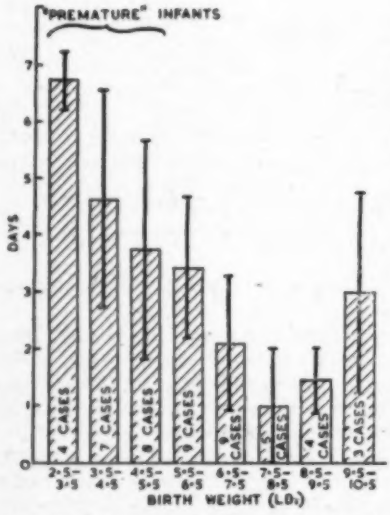

FIG. 2.—Relation between the birth weight of infants and the day on which the maximum plasma bile pigment concentration occurs. The average for each group is shown as a column, and the limits of one standard deviation are shown as a vertical line.

Type of Pigment.—The type of bile pigment found in the plasma of newborn babies was determined chromatographically in more than 40 plasma samples from 10 babies in whom the plasma pigment concentrations were over 7 mg. per 100 ml. The predominant pigment in every instance behaved on the chromatogram like bilirubin. The minor amounts of direct-reacting bile pigments have not been estimated quantitatively, but they appear to be about 5–10% of the total, or less. In some instances of high bile pigment concentration rather large quantities, probably 10–20%, of direct-reacting bile pigments were observed during the phase of decline of the total plasma bile pigment.

Discussion

This study serves to emphasize three aspects of bile pigment metabolism in the newborn infant. Firstly, although clinical reports have often suggested that jaundice is more common among premature infants, an examination of Fig. 1 shows that the presence of a great excess of bile pigment is characteristic of small newborn infants. Among these infants high concentrations of bile pigment occur in the plasma with a consistency which has not been reported previously. Thus of 11 babies weighing less than 4.5 lb. (2 kg.) at birth 9 had plasma pigment concentrations of over 12 mg. per 100 ml. at some time during the neonatal period, and five reached levels of 15 mg. or higher. The tendency for low birth weight to predispose to high plasma pigment concentration holds true throughout the range of birth weights of 3 to 9 lb. (1.4 to 4 kg.) even though there is considerable variation within some of the individual groups. Nevertheless, instances of high bile pigment among babies of normal weight are much less frequent than among the small babies, in whom it predominates. Thus, excluding haemolytic disease, hyperbilirubinaemia in the newborn is essentially a condition of infants of subnormal weight. The same tendency is expressed, in a minor way, in infants of normal weight.

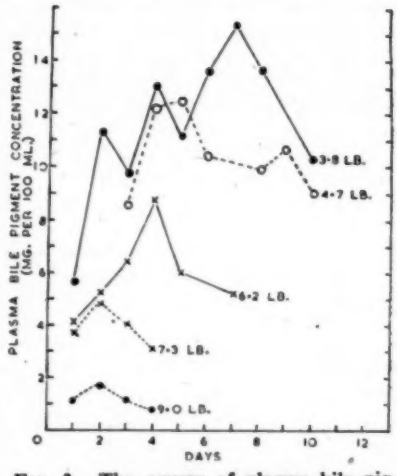

FIG. 3.—The course of plasma bile pigment concentration during the neonatal period of five "typical" babies of varying birth weights.

The series of infants have also been examined with regard to the length of the gestation period. The results are very similar to the analysis by birth weights, but in a small series no distinction can be drawn between the effects of age and those of growth of the foetus.

These elevated pigment levels in small babies were reached partly as a result of a more rapid rise of pigment, but also by a prolongation of the phase of rising pigment, as shown by the peak day in Fig. 2. The time required for return to a lower level of pigment after the peak had been reached was also more prolonged among the smaller babies, as exemplified in Fig. 3. Thus the tissues of small infants are exposed to higher concentrations of bile pigment for a longer period than are those of larger babies.

Secondly, when the type of pigment is taken into consideration it is clear that the neonatal period of the small newborn infant forms a second category, additional to haemolytic disease of the newborn, in which the tissues are exposed to large amounts of bilirubin. Claireaux *et al.* (1953) have commented on the significance of the fact that in neonatal haemolytic disease there occur much greater concentrations of plasma bilirubin than are found in the adult. High plasma bilirubin is very exceptional in the adult, since the predominant pigment of obstructive jaundice differs from bilirubin. Billing (1954) has shown that in these cases the amount of indirect-reacting pigment—that is, bilirubin—seldom exceeds 7 or 8 mg. per 100 ml. In adult cases of haemolytic jaundice this level is very rarely reached. The

greatly increased concentration of plasma bilirubin in neonatal haemolytic disease is undoubtedly of importance in the development of brain jaundice, and this may also be true of the substantial amounts of pigment which have now been shown to occur in premature infants unaffected with haemolytic disease. Claireaux *et al.* (1953) suggested that the time taken for the accumulation of the bilirubin in the non-haemolytic form of neonatal jaundice might account for the fact that these babies tend to die about the seventh day rather than on the second, as do those affected with brain jaundice due to haemolytic disease. It remains to be seen, of course, what factors other than plasma bilirubin concentration may affect the degree to which bilirubin penetrates the "premature" and "normal" newborn brain.

Thirdly, the degree of bilirubinaemia occurring in most of the small infants indicates that there usually exists a much greater defect of bilirubin metabolism than has previously been suggested. In recent years the conception that neonatal jaundice is not haemolytic in origin has gained much ground since the demonstration by Mollison (1948) that in the newborn infant there is no greatly elevated rate of erythrocyte disappearance to which the jaundice could be ascribed. More recent studies of normal infants (Fashena *et al.*, 1950) and of premature infants (Arthurton *et al.*, 1954) have confirmed this. The accumulation of bilirubin in the plasma is now usually attributed to a reduced excretory capacity of the newborn liver, though the degree of reduction is seldom sufficiently emphasized.

It is possible to compare the excretory ability of the small newborn infant with that of the normal liver, as estimated indirectly by Weech *et al.* (1941) in the human, and directly by Billing and Weinbren (1954) in experimental animals. From these studies one may calculate the normal rate of excretion of bilirubin when the plasma pigment concentration is 10 mg. per 100 ml., an amount which occurs frequently in small newborn infants. In the course of ten hours the normal liver can excrete an amount of bilirubin equivalent to all the haemoglobin in the body. The daily production of bilirubin by a newborn infant would be disposed of in fifteen minutes. Thus, under these circumstances, the liver of a small newborn infant can excrete bilirubin at a rate of only 1 or 2% of the normal adult liver.

This very low level of excretory activity of the liver of small newborn babies cannot be explained by some general factor such as reduced circulation or involution of the left hepatic lobe (Emery, 1953), since if all the liver functions were affected to this extent life could not be supported. The fundamental hepatic defect of non-haemolytic jaundice of the newborn must therefore have a highly specific character, probably confined to the immediate metabolism of bilirubin.

A possible explanation of the character of this defect is suggested by the fact that the high concentrations of plasma bilirubin are associated with only minor amounts of the direct-reacting bile pigments. This contrasts with experiments in which comparable plasma concentrations of bilirubin were maintained by intravenous injection of rats and rabbits. In these a substantial proportion of direct-reacting bile pigments, chiefly pigment I, also appeared in the plasma (Cole *et al.*, 1954; Billing, 1954). This suggests that the transformation of bilirubin to the direct-reacting bile pigments is greatly limited in the newborn baby. Malloy and Lowenstein (1940), as a result of a study of a strain of congenitally jaundiced rats, have proposed that this alteration of the indirect-reacting bilirubin to direct-reacting bile pigment is a prerequisite for the excretion of bilirubin by the liver. Such a chemical change probably would have the degree of specificity which is required to explain the presence of a great deficit in bilirubin metabolism while other liver functions remain relatively unimpaired.

The general features and mode of development of the non-haemolytic form of neonatal jaundice appear to be the following. During the period of intrauterine life bilirubin is removed across the placenta (Findlay *et al.*, 1947). Under normal circumstances, as seen in the large infant, the impending loss of this route of disposal at birth is anticipated by the development of an adequate excretory function of the liver during the later weeks of foetal existence. It is this development which is uncompleted in the small newborn infant. Thus "physiological" jaundice is not to be interpreted as an indication of rapid adjustment after birth, as has been claimed, but arises from lack of development before birth. This is the reason why it is characteristic of the newborn infant whose foetal growth has been interrupted by early delivery or retarded by adverse conditions. It is essentially abnormal rather than "physiological."

Summary

It is characteristic of prematurity that there is a high concentration of bile pigment in the plasma during the neonatal period. The influence of birth weight on the amount of pigment extends throughout the range of birth weights of 3 to 9 lb. (1.4 to 4.1 kg.), and is most fully expressed among small infants. In these the plasma pigment concentration often rises to 12 mg. per 100 ml. or above. Under these circumstances the liver's capacity to excrete pigment is estimated to be 1–2% of normal.

The plasma bile pigment has been shown to be bilirubin. The specific defect of bile pigment metabolism in the newborn infant may be a reduced capacity of the liver to transform bilirubin to direct-reacting bile pigment.

Prematurity is thus a second condition in which the tissues are exposed to high concentrations of bilirubin.

We are grateful to the medical and nursing staff of Queen Charlotte's Hospital for their co-operation in this study. Our gratitude is due to Miss O. B. Sweet, who carried out the laborious task of securing specimens for analysis.

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A new employment centre for the elderly of Finsbury was opened by Lord HORDER on November 11 at a ceremony presided over by the Mayor. Lord Horder said that he was happy to know that the new centre was to be called "Brooke House" as a well-deserved compliment to his old friend Dr. BLYTH BROOKE, medical officer of health for the borough, to whose enthusiasm this project was largely due. It was common knowledge, Lord Horder went on, that we were an ageing population, but there were now hundreds of thousands of men and women who, at an age which even 10 years ago would have marked them down as too old for any activity, were able to make a contribution, not only to their own health and happiness, but to that of the community. The human machine was very like a factory—it needed to be kept going by work. By denying elderly people the opportunity to do the work for which they were fit the community lost some useful service, and the people themselves, owing to lack of employment, aged more quickly. The centre, managed by the Employment Fellowship in co-operation with the borough council, employs 86 old people, of average age 72.

ACTION OF PROMETHAZINE ON SYSTEMIC BLOOD PRESSURE, PULMONARY ARTERY PRESSURE, AND PULMONARY BLOOD-FLOW

BY

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Since the report of Winter (1948) that some antihistamine drugs potentiate the hypnotic effect of barbiturates in animals, the former have been used with increasing frequency by anaesthetists (Beard, 1954). Promethazine hydrochloride ("phenergan") has been administered alone or in association with a barbiturate or pethidine as a sedative before cardiac catheterization, and it therefore seemed necessary to determine the effects of the drug on the circulation. This paper reports the results of the investigation.

Material and Methods

Six cases undergoing cardiac catheterization for diagnostic purposes were investigated: three had mitral stenosis, in two an atrial septal defect was confirmed, and in one with a dilated aorta no abnormality was found. Promethazine hydrochloride in doses of 50 or 25 mg. was administered by intravenous injection. The premedication is shown in the Table.

Pulmonary artery and brachial artery pressures were measured continuously throughout the observations using capacitance manometers. Simultaneous samples were taken at intervals from pulmonary and brachial arteries for blood gas analysis. In Case 3 the pressure measurements and blood samples were taken from the outflow tract of the right ventricle. Oxygen consumption was measured by breathing air from a spirometer of "box-bag" type (Donald and Christie, 1949); two observations were made in each case—one during the control period before the injection of promethazine, and one after the last blood samples had been taken. The second estimation was used to calculate the pulmonary blood-flow after administration of the drug. The heart rate was estimated from an electrocardiogram taken simultaneously throughout the observations.

The patients were supine, with one or two pillows under the head. The control period lasted approximately 20 minutes in each case, and the experimental period was continued for from 17 to 22 minutes after injection of the drug.

Results

The results are shown in the Table. The data obtained after injection of promethazine are presented as average readings over four five-minute periods: from 2 to 7, 7 to 12, 12 to 17, and 17 to 22 minutes after the injection.

No significant change in systemic blood pressure occurred after injection of the drug. Changes in pulmonary artery pressure were small, though a slight rise occurred in Case 5. Changes in oxygen consumption were small over the short period of the observations, values tending to increase in four cases, decrease in one, and remain unchanged in one. In the three cases with mitral stenosis and the patient with the dilated aorta, changes in arteriovenous oxygen difference were slight and the calculated cardiac output showed little change. In the two cases with atrial septal defect the arteriovenous oxygen difference decreased strikingly in one case, but showed a small increase in the other. Calculated pulmonary blood-flow therefore increased considerably in the former and decreased slightly in the latter. The heart rate increased slightly or moderately in all six cases.

An excellent hypnotic effect was obtained in Cases 1 to 4. Cases 1, 3, and 4 were already quiescent from soluble sodium amylobarbitone, but promethazine injection resulted in greatly increased sedation. In Case 2 adequate sedation was obtained from promethazine alone. Cases 5 and 6 were becoming restless before the administration of promethazine; after the injection some increase in sedation occurred, but this was accompanied by disorientation and inability to co-operate.

Discussion

For the purposes of the investigation of circulatory function or the premedication of cases with considerable cardiac disability, it is an advantage to use a sedative which produces the necessary hypnotic effect without appreciably altering the circulatory state. Promethazine hydrochloride has been shown to produce little effect on the circulation, apart from mild tachycardia, in six cases undergoing cardiac catherization. In addition, promethazine has been shown in animals to have a quinidine-like action in lengthening the refractory period of the auricles (Hutcheon, 1953), and may therefore be of value in the prevention of cardiac arrhythmias. It appears, however, that some sedative in addition to promethazine may be necessary in the restless or apprehensive subject.

Case No.	Diagnosis	Age, Sex	Premedication	Dose of Promethazine (mg. i.v.)	Pulmonary Artery / Brachial Artery Pressure (mm. Hg)					Arteriovenous O_2 Diff. (ml./l.)					Oxygen Consumption (ml./min.)		Heart Rate				
										Pulmonary Blood-flow (l./min.)											
					Control	2–7′	7–12′	12–17′	17–22′	Con.	2–7′	7–12′	12–17′	17–22′	Bef.	Aft.	Con.	2–7′	7–17′	12–17′	17–22′
1	Dilated aorta, S.R.	27 M	Sod. amylobarbitone 3 gr. per os	25	19/6 120/76	19/6 117/76	21/7 113/78	19/6 110/76	—	40 6·3	37 7·5	37 7·5	38 7·3	—	250	276	80	94	92	93	—
2	A.S.D., S.R.	15 F	None	25	15/7 125/80	14/6 120/83	16/8 120/83	16/8 122/82	14/6 —	17 15·1	17 14·8	18 14·0	18 14·0	21 12·0	257	252	94	105	106	110	106
3	M.S., S.R.	20 F	Sod. amylobarbitone 3 gr. p.o.	50	34/1* 125/64	33/1* 129/68	34/2* 128/64	35/2* 136/68	— —	40 5·7	46 6·0	52 5·3	48 5·8	— —	229	276	71	90	92	102	—
4	A.S.D., S.R.	18 M	Sod. amylobarbitone 3 gr., pronestyl 1 g. p.o.	50	18/7 107/65	18/7 105/65	17/6 109/64	18/6 112/63	18/7 109/65	28 9·0	30 8·1	34 7·1	— —	20 12·1	252	242	92	112	110	110	110
5	M.S., A.I., S.R.	44 M	Sod. amylobarbitone 3 gr. p.o.	50	28/11 103/67	33/16 110/67	39/19 111/68	38/18 111/69	36/17 112/69	46 6·0	— —	49 6·2	— —	55 5·5	278	302	66	68	73	74	76
6	M.S., A.F.	47 F	Sod. amylobarbitone 3 gr. p.o.	50	50/24 166/98	53/25 166/98	53/25 167/98	52/25 170/98	52/25 170/100	60 3·6	— —	— —	64 4·0	60 4·2	213	253	80	80	88	86	88

* Right ventricular pressures. A.S.D. = Atrial septal defect. A.F. = Auricular fibrillation. A.I. = Aortic incompetence. M.S. = Mitral stenosis. S.R. = Sinus rhythm.

Summary

The effects of intravenous injection of 25–50 mg. of promethazine hydrochloride have been studied in six cases undergoing cardiac catheterization. No significant changes occurred in the systemic blood pressure. One case showed a slight rise in pulmonary artery pressure. Pulmonary blood-flow showed little change in four cases, an increase in one, and a slight decrease in one. The heart rate increased in all cases.

The small circulatory changes associated with a satisfactory hypnotic effect suggest that promethazine is a suitable drug for the premedication of cardiac cases.

We are indebted to the technical staff of the Institute of Cardiology for assistance in making these observations.

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CARCINOMA OF THE BRONCHUS WITH BENCE JONES PROTEINURIA

BY

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Since the first description by Henry Bence Jones (1848) of the substance which now bears his name, interest has continued in the nature of Bence Jones protein. Its association with conditions other than multiple myelomatosis has only rarely been reported. Geschickter and Copeland (1928), from their own experience and a review of the literature, collected 26 cases of Bence Jones proteinuria in diseases other than multiple myelomatosis. Nine of these cases had skeletal metastatic tumours. Copeland (1931) reported three cases of carcinoma of the breast with skeletal metastases in which Bence Jones proteinuria was demonstrated. There have been few reports in recent literature, and Snapper (1949), from his own experience, believed Bence Jones proteinuria to be almost pathognomonic of multiple myelomatosis.

The two cases reported here are cases of carcinoma of the bronchus, confirmed at necropsy, in which Bence Jones proteinuria was demonstrated. An additional interesting feature was the sternal marrow of the first of these cases, which showed a " myeloma-like " picture.

Case 1

A man aged 74 had been for some time in poor health, complaining of anorexia and general malaise. Two months before admission to hospital he had noticed an exacerbation of his chronic cough with the production of a moderate amount of purulent sputum. Two weeks before admission his condition had deteriorated and he had developed feverishness and a sore throat. There was no relevant family or previous medical history. On October 6, 1952, he was admitted to Crumpsall Hospital, Manchester, under Dr. M. D. Milne. Examination revealed an emaciated ill man, sweating slightly. His temperature was 100.2° F. (37.8° C.), pulse 112 and regular, and B.P. 120/65. His heart was normal. There were diminution in expansion, dullness to percussion, and diminished air entry over the right lower lobe. The oral mucosa was inflamed. There was no hepatomegaly or splenomegaly and no lymphadenopathy.

Investigations.—Urine : S.G., 1012 ; Fehling's, Benedict's, and Rothera's tests were negative. Testing for albumin revealed a moderate amount of Bence Jones protein. The methods for detection of Bence Jones proteinuria outlined by Jacobson and Milner (1944) were used both in this and in the following case. *X*-ray examination of the chest showed right-lung collapse together with a large cavity with a fluid level, the appearances being those of a breaking-down neoplasm. Antero-posterior and lateral views of the skull showed no abnormality. Blood : Hb, 8.5 g. ; white cells, 13,300 (polymorphs 84%, lymphocytes 10%, monocytes 6%). The sputum was negative for tubercle bacilli. Serum urea was 54 mg. per 100 ml., serum protein 5.5 g. per 100 ml. (albumin 2.8 g., globulin 2.7 g.), serum calcium 7.5 mg. per 100 ml., serum inorganic phosphate 2.6 mg. per 100 ml.

Sternal Marrow.—The marrow smear showed an average cellularity and a normoblastic erythropoiesis. The striking feature was the preponderance of plasma cells, which formed about 40% of the nucleated cells. Many were atypical, having two and occasionally three nuclei. In addition many reticulum cells were present. The picture was thought to represent the reaction of the marrow to malignant infiltration, though clumps of tumour cells were not demonstrated and sections of marrow fragments gave no diagnostic assistance.

Clinical Course.—Treatment with antibiotics failed to alleviate a short downhill course, and the patient died on December 10.

Necropsy Findings.—The right lung weighed 2,100 g. A large growth arising from the right main bronchus had extended throughout most of the right lung. Areas of necrosis, dilated bronchi containing pus, and a right-sided empyema were present. Both kidneys and the right adrenal contained tumour secondaries. Microscopy of the primary and secondary tumours showed an anaplastic oat-celled carcinoma.

Case 2

A man aged 40 had been for three months in poor health associated with loss of weight and lack of energy. He complained of dyspnoea and a non-productive cough ; there was no haemoptysis. One brother and a sister had died of pulmonary tuberculosis. His previous medical history was not relevant. On March 6, 1953, he was admitted to Crumpsall Hospital, Manchester, under Dr. R. W. Luxton. Examination revealed a pale ill man ; temperature 98° F. (36.7° C.), pulse 88 and regular, B.P. 130/80. His heart was normal. Trachea to right, diminution in expansion, percussion note and air entry over both bases. The liver was enlarged 2 in. (5 cm.) below the costal margin ; the spleen was just palpable ; there was no lymphadenopathy.

Investigations.—Urine : S.G., 1020 ; Fehling's, Benedict's, and Rothera's tests were negative. Testing for albumin revealed a moderate cloud on boiling and with sulphosalicylic acid. Subsequent investigation revealed in addition to albumin the presence of a moderate amount of Bence Jones protein. *X*-ray examination of the chest showed partial consolidation of the right middle lobe, the appearances suggesting a neoplasm. The patient's condition precluded further radiological examination. Blood : Hb, 11.5 g. ; white cells, 11,000 (polymorphs 73%, lymphocytes 12%, eosinophils 3%, basophils 1%, monocytes 6%, myelocytes 5%) ; normoblasts, 3 per 100 white cells. The sputum was negative for tubercle bacilli. Serum proteins, 5.7 g. per 100 ml. (albumin 2.6 g., globulin 3.1 g.) ; serum alkaline phosphatase, 17 King–Armstrong units per 100 ml. Unfortunately, specimens of urine and serum were several weeks old when submitted for electrophoresis and, although kept frozen solid, did not give satisfactory electrophoretic patterns.

Sternal Marrow.—The marrow smear showed a depression of erythropoiesis associated with the presence of many undifferentiated cells resembling reticulosarcoma or anaplastic carcinoma. Clumps of tumour cells were not demonstrated, nor did section of marrow fragments give additional information.

Clinical Course.—Deterioration was rapid; the patient developed purpura, haemoptysis, and epistaxis, and died on March 19.

Necropsy Findings.—The right lung weighed 1,010 g. The bronchus to the right middle lobe was occluded by a mass of whitish growth 3 by 2 cm. in diameter. The remainder of the right lung and the left lung were not involved in growth. The liver weighed 5 kg. and showed widespread secondary deposits, as did the pancreas. Microscopy of primary and secondary tumours showed an oat-celled carcinoma. Section of the sternum revealed metastatic carcinoma.

Discussion

The main interest of the two cases is that they provide further unequivocal instances of the occurrence of Bence Jones proteinuria in secondary carcinomatosis. Both were cases of bronchial carcinoma of oat-cell type accompanied by secondary deposits in bone. Study of previously reported cases of Bence Jones proteinuria in skeletal secondary carcinomatosis does not indicate any special association with bronchial carcinoma.

Case 1 further illustrates that multiple myelomatosis may on occasion be simulated by secondary carcinoma if undue reliance is placed on the finding of Bence Jones proteinuria together with the presence of a high percentage of plasma cells in the marrow smear. That carcinoma cells infiltrating marrow can arouse a plasma-cell response is well known, and several recent papers have emphasized the occurrence of a "myeloma-like" marrow reaction in such cases. Rohr and Hegglin (1936), Nordenson (1940), Stöger (1941), and Delcourt (1946) have all reported this association. Coste *et al.* (1948) described a case under the heading "Pseudo-maladie of Kahler," while Marchal and Mallet (1948) reviewed the subject under the heading "Plasmacytose Cancereux." Hardisty (1952) published a further case in which metastatic breast cancer gave a marrow picture indistinguishable from that of myelomatosis.

The possibility that multiple myelomatosis and carcinoma of the bronchus may have coexisted in these two cases requires consideration. In both cases microscopical examination of post-mortem material showed generalized carcinomatosis. In addition to the histological study of the primary tumour, sections were taken in Case 1 of adrenal, kidney, and sternum, and in Case 2 of liver, spleen, kidney, sternum, and vertebrae. In each case the pathology was typical of secondary carcinoma, with no histological evidence to support a diagnosis of multiple myelomatosis.

The validity of methods for the detection of Bence Jones protein has occasioned much discussion. Snapper (1949), in a brief review, said that the careful examination, under controlled conditions of temperatures, of precipitation and solution affords the most suitable method for the routine examination of urine for this substance. The methods outlined by Jacobson and Milner (1944) and recommended by Snapper were followed in the examination of the above cases. In each case a substance fulfilling the criteria laid down by these authors was demonstrated. Temperatures of precipitation were from 50 to 55° C., whilst the precipitate was completely redissolved at a temperature of 100° C.

It is interesting to note the increase in serum globulin in both these cases. Such an increase was reported by Delcourt (1946) in a case of metastic abdominal cancer in which the globulin was 3.8 g. per 100 ml. Coste *et al.* (1948) describe a case of breast cancer in which the globulin was also 3.8 g. per 100 ml. In their case the myelogram showed that plasma cells formed 80% of the nucleated cells. The sternal marrow of Case 1 had the characteristic appearance associated with multiple myelomatosis, and this case adds further weight to the growing opinion of the non-specific nature of such a marrow picture.

Summary

Two cases of carcinoma of the bronchus with Bence Jones proteinuria are reported.

The simulation of multiple myelomatosis is commented upon.

Alternative explanations of the findings are discussed. The literature is briefly reviewed.

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ACUTE SUPRARENAL FAILURE

BY

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The occurrence of acute suprarenal failure in cases of Addison's disease is not uncommon, but in cases in which previous adrenal insufficiency was unsuspected it is not very usual. The following case is reported because of its interest, as there were practically no signs or symptoms of suprarenal failure until within five days of the patient's death.

Case Report

A man aged 30 was seen on September 8, 1953, with a history of loss of weight for one year (approximately 1 st.—10.9 kg.), lassitude, some dizziness, and a feeling of faintness for the last three months. He had previously had a tuberculous lesion of the left knee, which had responded well to treatment, there having been no evidence of any pulmonary lesion at that time. In view of the lassitude and loss of weight, the possibility of reactivation of the knee or of a pulmonary tuberculous lesion was considered. There was no evidence of active disease in the knee either clinically or radiologically, this being confirmed by an orthopaedic surgeon, but an *x*-ray examination of his chest showed a minimal lesion at the left apex. The clinical findings were negative apart from limitation of range of movements of the left knee. His blood pressure was 130/85, he had no sputum to test, but his stools did not contain tubercle bacilli. The rapid onset of further symptoms prevented gastric lavage from being done. His E.S.R. at this time was 20 mm. in the first hour (Westergren).

It was thought that the loss of weight and the lassitude were probably accounted for by the tuberculous lesion in the chest, although at the time it was felt that the lesion was not sufficient to cause such toxic symptoms. The patient was put on to streptomycin, 1 g. twice a week, P.A.S., 12 g. daily, and isoniazid 150 mg. twice daily. Forty-eight hours after starting this regime vomiting began, but his general condition appeared to be good. Vomiting continued the following day (September 20), and as this was thought to be probably due to the P.A.S. that drug was stopped. On September 21 his general condition rapidly deteriorated; he became dehydrated, felt thirsty, had marked oliguria, and his blood pressure had dropped considerably, being only 95 systolic, the diastolic pressure not being readable. His alkali reserve was 24 vols. CO_2 and his chlorides 450 mg. per 100 ml. as sodium chloride. His blood urea was 100 mg. per 100 ml.

The probability of the condition being an acute Addisonian crisis was considered, and his suprarenals were *x*-rayed, but there was no definite calcification in this area. He was given a glucose-saline drip, but as the response was poor and his general condition unsatisfactory he was put on to cortisone and "eucortone" (50 mg. of cortisone 12-hourly and 20 ml. of eucortone into his intravenous drip every three hours). Marked clinical improvement was now seen, his blood pressure, which had fallen to 60 mm. Hg systolic, rising to 140 mm., and between 80 and 90 diastolic. During the first twelve hours of this treatment his fluid intake was 4,400 ml. while his total loss by vomiting and urine was 310 ml. During the next twelve hours his total intake was 2,600 ml. and his total output 2,325 ml. This initial high intake and poor output was due to his extremely dehydrated condition; but, unfortunately, his general condition, which had at first improved rapidly, began to deteriorate during the next twenty-four hours, and his blood pressure fell again, his urine output decreased, and by midnight on September 22 his blood pressure had fallen to 80/60. Cortisone was thereupon increased to 50 mg. six-hourly, which resulted in a further temporary improvement in blood pressure to about 120/80, but his urine output, which had fallen, did not improve. Fluid intake on September 22 was 5,500 ml. while the output was 1,900 ml. This was accompanied by changes in the lungs, where there was evidence of marked engorgement, both clinically and radiologically, particularly on the left side. He died on September 23.

Biochemical Findings.—Blood urea on admission (September 15) 27 mg. per 100 ml.; blood count normal; Hb, 107%; white cells, 8,000 (polymorphs 67%, lymphocytes 32%, hyaline cells 1%); E.S.R., 20 mm. in first hour. On September 21, after the initial vomiting, the blood urea was 100 mg. per 100 ml., his alkali reserve was 24.2 vols. CO_2, and his plasma chlorides as sodium chloride 450 mg. per 100 ml. The following day his alkali reserve was 31.9 vols. CO_2 and plasma chlorides as sodium chloride 505 mg. per 100 ml; the blood urea was 68 mg. per 100 ml. During this time the urinary chlorides were: September 21, 8.15 p.m., *p*H 5.0, chlorides 238 mg. per 100 ml.; September 22, 1.30 a.m., *p*H 4.8, chlorides 278 mg. per 100 ml.; 8 a.m., *p*H 5.0, chlorides 350 mg. per 100 ml.; September 23, serum potassium 22 mg., serum sodium 295 mg. per 100 ml.

Post-mortem Examination.—This showed no abnormality apart from the lungs and suprarenals. Both lungs were adherent to the parietal pleura; the left lung was greatly enlarged and of a rubbery consistence, exuding frothy fluid. Numerous haemorrhages were present on the pleural aspect; and the upper lobe, on section, contained a caseous encapsulated nodule, about 15 mm. in diameter. There were greyish-white trefoil areas scattered throughout the lungs, suggestive of miliary tuberculosis. The right lung was similar to the left but less voluminous, and it also contained an apical upper-lobe lesion about 1 cm. in diameter. The liver was congested; the spleen was one and half times its normal size, moderately firm; the left suprarenal was grossly enlarged, indurated, and distorted in shape, and was completely replaced by an opaque, caseo-calcareous tuberculous lesion. The right suprarenal was adherent to the liver and four times its normal size, and also replaced entirely by fibro-caseous tuberculosis.

Histology.—There was fibro-caseous tuberculosis in both lungs, with a moderately well defined fibroblastic "capsule," and with new tubercle formation elsewhere in the lung. The suprarenals were completely replaced by caseo-calcareous disease, and the sections were too friable and broke up on cutting. Remnants of the sections, however, showed caseo-calcareous debris and fibro-granulomatous tuberculosis.

Discussion

This case is interesting because of the abrupt onset of suprarenal failure, especially as at necropsy the patient's suprarenals appeared to have been completely replaced by tuberculous caseous material, and it is surprising that there was no previous stage when there were signs of a relative insufficiency. Doubtless the lassitude complained of was associated with this, but there were no corollary signs such as a lowering of the blood pressure or pigmentation of the skin to help in the diagnosis, and the minimal chest lesion might have accounted for this lassitude. A further difficulty, which delayed the giving of cortisone for just over twenty-four hours, was the onset of vomiting shortly after P.A.S. had been started, and which was therefore thought to be due to this drug, especially as during this period the blood pressure remained up. Valuable time was consequently lost before cortisone was given, and the patient became dehydrated. It is possible that as the P.A.S. was given in the soluble form it may have upset the potassium balance, causing the acute onset, or, again, the P.A.S. may have caused vomiting, leading in turn to dehydration, with some alkalosis, which might have been the precipitating factor.

It would appear from this case that the amount of suprarenal tissue necessary for maintaining a practically normal life must be very small, since the tuberculous process must have been present for some months.

Summary

A case of acute suprarenal failure is described, due to destruction of the suprarenals by a tuberculous process, there being no evidence of suprarenal failure previously. Difficulty in arriving at an accurate diagnosis was encountered because of a minimal chest lesion, which might have accounted for the patient's symptoms, and the treatment with cortisone was delayed, as the vomiting, when it started, was thought to be due to P.A.S.

THROMBOCYTOPENIA FOLLOWING SULPHADIMIDINE

BY

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Sulphadimidine is generally, and with good reason, regarded as one of the safest of the sulphonamide drugs. Thrombocytopenia is one of the rarer manifestations of sulphonamide toxicity. Its occurrence after sulphadimidine administration has not previously been recorded.

Case Report

A boy aged 3 was admitted to the Duchess of York Hospital for Babies, Manchester, on January 18, 1954. He was the fifth child of healthy parents and, except for chicken-pox in November, 1953, had always been well. Twelve days before admission he developed an upper respiratory infection with cough and sore throat. A mixture containing sulphadimidine was given in a dose of 1 g. twice a day, along with a cough mixture (mist. codein. pro infant. (*N.F.*), 2 dr. (7 ml.) thrice daily). The symptoms subsided, but the mother continued the sulphonamide mixture for seven days. The day after it was stopped the boy became hot and flushed with a temperature of 104.6° F. (40.3° C.). At the same time a rash appeared on the shoulders. The sulphadimidine was prescribed once more, and the mother, not realizing that it was the same medicine, also gave what was left of the original mixture. For four days the child had 4 g. of the drug daily. During this period the rash spread all over the body, anorexia was very marked, and the child was constipated. He also became drowsy and was unable to stand because of dizziness. On the day before admission a swelling appeared in the right side of the neck.

On the day of admission his breathing was rapid for short periods. He passed only small amounts of urine, without pain and with no obvious haematuria.

On admission he was drowsy and fretful, lying curled up when left alone. There was a widespread morbilliform rash, and the face was flushed. Two small bruises were noted in the lumbar region. Many glands were palpable in the neck, and on the right side there was a large soft swelling overlying the middle of the sterno-mastoid muscle and extending forward over the angle of the lower jaw. The axillary and inguinal glands were also palpably enlarged. The liver edge was palpable two fingerbreadths below the costal margin. No other abnormalities were discovered.

A provisional diagnosis of sulphonamide toxicity was made and penicillin administration was begun in a dosage of 1.5 mega units daily. Potassium citrate was also given in a daily dose of 6 g., and the fluid intake was pushed to 2 pints (1,140 ml.) a day. The haematological findings are summarized in the Table.

On the second hospital day the boy's temperature rose to 103° F. (39.4° C.). He was passing urine plentifully—21 oz. (200 ml.) plus two wet beds in the first 24 hours—and drinking freely, but remained very drowsy. The urine contained a trace of albumin, but no red cells or crystals were found; the chemical test for sulphonamides was strongly positive. In the afternoon of this day he passed a very large tarry stool which gave a strongly positive benzidine reaction.

The temperature settled within 12 hours, and in the course of the next few days the child became brighter and more

Haematological Findings

Date	Hb	W.B.C.					Platelets
		Total	Polymorphs	Lymphocytes	Eosinophils	Monocytes	
19/1/54	78%	3,980	66%	33%	—	1%	45,000
20/1/54	78%	4,600	48%	51%	—	1%	55,000
21/1/54		5,400	45%	53%	1%	1%	60,000
22/1/54		6,300	38%	60%	1%	1%	110,000
23/1/54		8,700					135,000
25/1/54		12,600					275,000
26/1/54		9,600					360,000
27/1/54	74%	9,000	55%	42%	—	3%	400,000

alert, the rash gradually faded, and the lymph-node swelling subsided. Melaena stools were passed for three days, but on the ninth day after admission the faeces gave a negative benzidine reaction. The urine never contained red cells or crystals, but the chemical test for sulphonamides remained positive until the third day.

A throat swab taken on admission gave a scanty growth of normal upper respiratory flora. A Paul–Bunnell test on the third day gave no agglutination and a 1:1,000 Mantoux test was negative. Chest *x*-ray films taken on admission showed slight enlargement of the right hilar shadow but no pulmonary lesion. Bone marrow was obtained on the second day in hospital by iliac crest puncture. There was definite hypoplasia—total nucleated cell count of 46,800 per c.mm. (normal for children of 2 to 10 years, 70,000–700,000 per c.mm.)—with general reduction in the number of all types of nucleated cells; myeloid/erythroid ratio 12:1 (normal ratio in children 4:1 to 13:1); megakaryocytes were plentiful—1% of the nucleated cells.

The child was finally discharged after 12 days in hospital in apparently normal health.

Discussion

This child received a total of 30 g. of sulphadimidine in 11 days. He had not, so far as his parents were aware, ever received a sulphonamide before, and there was no family or personal history of allergy or idiosyncrasy. The effects were presumably, therefore, a direct toxic action of the overdose. These effects were fever, rash, lymph-node enlargement, moderate granulocytopenia (total polymorph count of 2,600 per c.mm.), and marked thrombocytopenia. The last manifested itself by very slight bruising and profuse melaena. The cerebral state was probably also the consequence of sulphonamide intoxication.

Thrombocytopenia after sulphonamide administration has been infrequently reported. In 1943 Kracke and Townsend reviewed the literature and found reports of 10 cases, to which they added two of their own. Since then there have appeared reports of another 21 cases, making 33 in all. The drugs responsible were sulphanilamide, 4 cases; sulphapyridine, 8 cases; sulphathiazole, 12 cases; sulphadiazine, 7 cases; sulphamerazine, 1 case; and sulphafurazole, 1 case. The frequency with which preparations appear on this list reflects their popularity rather than their toxicity, and it is noteworthy that the number of reports, after reaching a peak in 1943, 1944, and 1945, has fallen off sharply—presumably following the more general use of penicillin and other antibiotics. It would appear that almost all of the more soluble and absorbable sulphonamides are capable of producing thrombocytopenia.

In the present case there was an obvious depression of the bone marrow affecting all elements. This was almost certainly due to the sulphonamide in view of the rapid recovery following withdrawal of the drug, the failure to discover any other cause, and the associated symptoms of sulphonamide toxicity. This case underlines the potential toxicity of even the best of the sulphonamides. It would appear to be advisable that these drugs be prescribed in quantities sufficient for a definite short period only, and that opportunities for excessive medication be not given to parents of patients by supplying more than is needed. The overdosage in this case arose from a misunderstanding, and though the outcome was favourable it might not have been.

I wish to thank Professor W. F. Gaisford for criticism and advice.

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Medical Memoranda

Treponematoses in Gambia: Preliminary Communication

Investigations have been made into the forms of treponematoses occurring in Gambia, and two forms have been encountered. These are yaws and another treponemal disease which shows many similarities with the endemic syphilis described among the Arabs and the people of Bosnia.

This second disease, as found in Gambia, usually appears first on the mucous membranes at the angles of the mouth in young children, or it can appear on the tip of the penis in small boys. These lesions contain large numbers of spirochaetes morphologically identical with *Treponema pallidum*, and the patients give strongly positive Wassermann and Kahn reactions. There is little doubt that the disease is mainly transmitted by the use of a common drinking-cup and, less often, by close personal contact. The use of a common drinking-cup is prevalent in Gambia, and the people themselves, when asked if the disease could be transmitted from one person to another, volunteered the information that they believed the drinking-cup to be responsible for passing on the disease.

The secondary manifestations of the disease which have been observed are (*a*) florid eruptions on the vulva and in the anal cleft, and (*b*) circularly arranged groups of papules which may coalesce to form rings; these can occur on any part of the skin. These lesions contain large numbers of spirochaetes.

The most common tertiary lesion observed is a hyperkeratosis of the palms and soles associated at a later stage with depigmentation of the hands and feet. Destructive lesions of the nasal septum are fairly common, but lesions of the long bones are rarely seen.

There are five main tribes in Gambia, and all cases of this disease which have been seen have been restricted to one tribe.

Gambia occupies a unique position in West Africa, as it lies on the fringe of the tropical rain-belt. The average annual rainfall in Gambia is 42 in. (107 cm.), with a dry season extending over eight months, while 45 miles (72 km.) to the south the rainfall is 73 in. (185 cm.), and 83 miles (134 km.) to the north the rainfall is 21 in. (53 cm.). The mean temperature in Gambia is 81° F. (27.2° C.). Therefore it is likely that the climatic conditions in Gambia, which are intermediate between those in tropical West Africa to the south and those in the desert to the north, are suited to the transmission of both yaws and the so-called endemic syphilis. This theory tends to be supported by the present observations on the occurrence of the two diseases side by side in a relatively small territory.

Our thanks are due to Dr. A. E. Wilkinson, of the M.R.C. V.D. Reference Laboratory, who undertook the serological investigations.

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General Peritonitis after Subgluteal Abscess

The following case is reported as no previous reference to such a case can be found in the literature.

CASE REPORT

A man aged 33 was admitted to hospital as an emergency case with a provisional diagnosis of general peritonitis due to a burst appendicular abscess. Twelve days previously he had gone to bed at home with fever and headache. Three days later, in addition to the fever which continued, he developed a pain in the left buttock. He called in his own doctor, who diagnosed influenza, which was prevalent at the time. Five days later his doctor saw him again. He was still feverish and the pain in the left buttock was worse and was thought to be due to sciatica. He was also constipated and was given a strong aperient, which caused a copious evacuation of the bowels two days later. The pain in the buttock continued to get worse, until on the morning of admission it suddenly disappeared. In the afternoon he developed stomach-ache, felt especially in the right iliac fossa and across the hypogastrium under the ribs. There was no vomiting or cough.

His previous medical history was that he had had a pyogenic folliculitis of the hair of the left leg for six months. This had now cleared up. In 1941 he had suffered from severe non-specific dysentery while serving with the Forces in West Africa. This was followed by a polyarthritis affecting especially the hip-joints. He was invalided out of the Forces, but had been quite well since working as a telephone supervisor.

On examination in hospital he was seen to be well built and well covered. He looked ill and had rapid gasping respiration. His temperature was 103.8° F. (39.9° C.), and pulse 114. His tongue was dry and the abdomen tender all over, but especially in the right iliac fossa. There was guarding of both recti, but no board-like rigidity. Examination per rectum was painful, but no mass could be felt. The left buttock appeared quite normal and was not tender on pressure. The movements of both hip-joints were full and painless.

At operation the same evening the abdomen was opened through a long right paramedian incision. The peritoneal cavity was found to contain a large quantity of frank yellow pus. Large quantities of pus were sucked from the right paracolic gutter and the pelvis. The appendix, duodenum, stomach, gall-bladder, and bowel were examined without revealing any abnormality. The abdomen was therefore closed with drains into the pelvis and below the right lobe of the liver. He made a good recovery with the aid of chemotherapy and intravenous fluids.

One week after operation he complained of a recurrence of the pain in the left buttock. Twelve days after operation there was a distinct tender swelling under the gluteus maximus between the great trochanter of the left femur and the sacrum. He was given a general anaesthetic and the fibres of the gluteus maximus were split to drain a large abscess cavity. On inserting a finger, the posterior surface of the neck of the femur was directly felt. *X*-ray examination of the bony pelvis and femurs showed no sign of osteomyelitis. A culture of the pus from the abscess grew anaerobic streptococci and the coliform organisms. One month later, when the incision in the buttock had healed, he developed a pelvic abscess, which was successfully drained per rectum. A culture of the pus grew non-haemolytic streptocci.

Three weeks later there was a recurrence of pain in the left buttock. The abscess was reopened and drained. Further radiographs showed no infective focus of bones. He then made rapid progress and was discharged home one month later, though the buttock incision was still discharging slightly.

He finally returned to work six months after the onset of the illness. Both hip-joints had full painless movements and there was no residual disability of any sort.

COMMENT

It seems probable that the general peritonitis in this case was caused by pus from the subgluteal abscess tracking along the left pyriformis muscle and bursting into the peritoneal cavity through the pelvic peritoneum. This probability seems strengthened by the fact that a pelvic abscess developed six weeks after the initial drainage of the peritoneal cavity, and shortly after the first external drainage of the abscess had ceased. Presumably a second overflow of pus reached the pelvis, where it was walled off before reaching the general peritoneal cavity.

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Torsion of Hydrosalpinx at 14 Years of Age

Torsion of the Fallopian tube, although not a rarity (de Soldenhoff, 1949), is still uncommon enough to be worth reporting. Wolf (1951) recorded that just over 120 cases had been described since 1890. Neel *et al.* (1943) saw torsion of the tube in a child aged 3 years. Tauber (1949) undertook a review of the subject of tubal torsion, and stressed that the history of repeated attacks of pain was the most significant feature. Shaw (1949) believed that the condition differed from torsion of an ovarian cyst in that "shock" was absent. Novak (1949), quoting Anspach, stated that a hydrosalpinx in childhood may be secondary to (*a*) vulvovaginitis, (*b*) one of the exanthemata, or (*c*) tuberculous infection.

CASE REPORT

A girl aged 13 years 8 months was admitted to hospital in June, 1952, complaining of colicky pains in the left iliac fossa for 13 hours. She had vomited four times. There was no disturbance of her bowel or urinary functions. She had suffered from most of the common exanthemata. There was no history of previous attacks of abdominal pain. Her mother stated that from infancy until a year previously the child had had repeated episodes of vulvar inflammation, without any discharge. It had always responded to bathing and the application of talcum powder. There was no relevant family history.

On examination the temperature was 99.4° F. (37.4° C.), pulse 92. Tenderness, guarding, and rigidity were present in the left iliac fossa. Rectal examination revealed no

abnormal findings. The white blood cells numbered 14,000 per c.mm. (86% polymorphs). A straight *x*-ray film of the abdomen and an intravenous pyelogram showed no abnormality. A catheter specimen of urine was sterile and the deposit normal.

Streptomycin, 0.5 g. twice daily, was prescribed for four days. The temperature was 100° F. (37.8° C.) on the morning after admission, but thereafter all signs and symptoms resolved. Six weeks later she was continuing well.

One evening in February, 1953, she was again admitted complaining of colicky pains, radiating from the left loin to the left iliac fossa. There was nausea and retching with each spasm of pain. Micturition caused lower abdominal discomfort. The bowels had acted normally. Menstrual history: 12, 5/30; regular; moderate flow; no dysmenorrhoea. Menstruation had started on the day of admission, three days later than expected.

On examination her temperature was 98° F. (36.7° C.), pulse 86. The cardiac apex beat was on the left. There was tenderness with guarding in the left loin and left iliac fossa. A provisional diagnosis of renal colic was made. Pethidine, 100 mg., and atropine sulphate, 1/100 gr. (0.65 mg.), were given by injection. The patient vomited once during the night. The next morning she still complained of colicky pains. Her temperature was 98.6° F. (37° C.), pulse 80. The tongue was clean. There was tenderness with guarding in the left iliac fossa. No area of dullness was detected on abdominal percussion. The vulva was normal and the hymen intact. On rectal examination no pelvic tumour or localized tenderness was detected. The white cells numbered 15,000 per c.mm. (92% polymorphs). A catheter specimen of urine was sterile and the deposit normal. A straight *x*-ray film of the abdomen showed no urinary calculus.

By that evening the patient had become flushed, the tongue was furred, the temperature 100° F. (37.8° C.), and pulse 120. There was acute tenderness in the left iliac fossa, with guarding and rigidity. Rebound tenderness had now developed.

Under a general anaesthetic it was possible to palpate a sausage-shaped tumour in the left iliac fossa. A right lower paramedian incision was made. The left Fallopian tube was found to be plum-coloured and grossly swollen, having twisted twice in an anti-clockwise direction. The left ovary was not involved in the torsion. The right tube and ovary, the uterus and the appendix were normal in appearance. No Meckel's diverticulum was found. A left partial salpingectomy and appendicectomy were performed. The patient's convalescence was uneventful. A gonococcal complement-fixation test was reported to be negative.

Pathological Report.—Macroscopically the specimen consisted of a contorted Fallopian tube, the tissues of which were swollen and of a deep purple colour. The dilated parts of the tube contained blood-tinged yellowish fluid. The medial 15 mm. of the tubal lumen was of normal dimensions, but gave place laterally to a uniformly dilated section 95 mm. long and 20 mm. in diameter. The mucous membrane lining this part showed longitudinal ridges representing the mucosal plicae. These were widely separated by intervening strips of smooth mucous membrane. At its lateral extremity a transverse septum separated this loculus from another, 20 mm. long and 15 mm. in diameter. This latter cavity was lined by smooth and shining mucous membrane and did not communicate with the peritoneal cavity. The tubal fimbriae, firmly matted together, were adherent to the peritoneal aspect of its wall.

Histologically, sections from all the areas examined showed much oedema combined with haemorrhage, especially in the subserous layer, moderate polymorphonuclear leucocytic infiltration, and recent venous thromboses. The arteries examined were all patent. Section of the medial end of the tube showed a normal mucosal pattern. Section of the wall of the lateral loculus showed a thin lining of fibrous tissue clothed with a single layer of cuboidal epithelium. The fimbriae had multiple points of fusion, one to another, indicative of past inflammation. No evidence of recent sepsis was seen in any section.

The findings were in keeping with torsion of a hydrosalpinx which had occurred long enough before operation to allow reactive polymorphonuclear infiltration to follow the oedema, haemorrhage, and venous thrombosis.

COMMENTS

The torsion of the Fallopian tube here reported was undoubtedly related to its pathological condition. The aetiology of the hydrosalpinx was not certain. The history of vulvitis was not conclusive. The first episode of pains in the left iliac fossa may have been due to a partial torsion of the normal tube, which settled down spontaneously, after causing enough tissue reaction to produce the hydrosalpinx. The intermittent colicky nature of the pain, and the absence of "shock" in torsion of the Fallopian tube not involving the ovary, were well illustrated.

My thanks are due to Professor Ian Aird and to Mr. R. H. Franklin, under whose care the patient was admitted, for permission to publish a report of this case, and to Dr. G. A. K. Missen for the pathology report.

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A Case of Bacterium Friedländeri Meningitis

The comparative rarity of this condition seems to justify publication of another case similar to that of Eberlie (1953).

CASE REPORT

A dock worker aged 48 was admitted to hospital on January 15, 1952, with a febrile illness of 10 days' duration, characterized by general malaise with headache and a troublesome cough with jelly-like sputum. There was nothing of note in his past history, except for an attack of nephritis in 1950, from which he had made an apparently complete recovery.

On admission his temperature was 103° F. (39.4° C.), pulse 80, and respirations 20. Sensorium lucid, but cerebration slow. Herpes labialis. Fauces injected. Tympanic membranes normal. Scattered rhonchi in lung fields. Neck rigidity and inability to kiss his knees. Pupils reacted to light and accommodation. Fundi normal. No cranial-nerve palsy and no other evidence of focal lesion in the nervous system. C.S.F. opalescent, containing an excess of pus cells and what appeared at first sight to be Gram-negative diplococci. Treated with sulphadimidine, 2 g. four-hourly for the first 24 hours, and then 2 g. six-hourly. The temperature fell by crisis, and on January 17 he was afebrile, much more alert, and appeared clinically to be well on the road to recovery. That day the laboratory reported that from the C.S.F. an organism had been grown with the cultural and morphological properties of *Bacterium friedländeri* (*Klebsiella pneumoniae*). A similar organism was cultured from the sputum. As the clinical condition of the patient had so greatly improved, it was decided to continue treatment purely with sulphadimidine, and the events justified this decision. The patient was, in fact, discharged home well on February 2, and when seen a month later at the follow-up clinic demanded to return to work. Before his discharge from hospital, radiographs of the chest showed no evidence of parenchymal involvement, and radiographs of the sinuses were also clear.

COMMENT

Thompson *et al.* (1952), in reporting a case of *Kl. pneumoniae* meningitis with bacteriaemia and pneumonia, made a careful review of the literature and analysed 118 cases, 31 with recovery. According to their Table 3, in the pre-sulphonamide era, of 60 cases only 4 recovered, but with sulphonamides alone, of 20 cases 9 recovered. With a combination of sulphonamides and penicillin, of 15 cases 9 recovered; and with sulphonamides, penicillin, and streptomycin, of 13 cases 7 recovered. It is noteworthy that with penicillin and streptomycin, alone or in combination, none recovered. On the other hand, one case (Martin and Sureau, cited by Bombardier, 1950) recovered with chloramphenicol treatment after failure of sulphonamides, penicillin, and streptomycin.

On theoretical grounds it would appear that the drug of choice in the treatment of *Bacterium friedländeri* meningitis is chloramphenicol, because of the ready attainment of therapeutic levels in the cerebrospinal fluid (Ross *et al.*, 1949; Hewitt and Williams, 1950). There is some evidence that oxytetracycline ("terramycin") also crosses the blood–brain barrier (Werner *et al.*, 1950), but aureomycin is known to be a poor drug for systemic administration in meningitic disease.

The case here reported did extremely well on sulphadimidine alone, and this shows that clinical judgment must remain, in the last analysis, the supreme arbiter, even in questions of treatment. Except when confronted with fulminating disease, I would renew a plea, made by Banks and others, for withholding intrathecal treatment with antibiotics in purulent meningitis until the bacteriological diagnosis and the clinical course of the disease show it to be imperative. Sulphonamides by the oral or parenteral route, when they do not effect a cure, always give time for deliberation and for completely informed final treatment.

My thanks are due to Dr. Martin Hynes for the bacteriological reports.

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Perforation of a Duodenal Ulcer into the Common Hepatic Duct: With Relief of Obstructive Jaundice

Gastro-intestinal biliary fistulae are not uncommon as a complication of cholecystitis and gall-stones. Kehr (quoted by Hicken and Coray, 1946) found them in 5% of 2,000 patients having an operation on the biliary tract. Perforation of a duodenal ulcer into the biliary tract, however, is very rare. Lønnerblad (1932) described a case and collected 11 others from the literature. Barclay (1936), Hicken and Coray (1946), Nivière (1947), and Vergoz and Lebond (1948) described and collected further cases from the literature, making 30 in all. The evidence in many of the reported cases is only radiological—that is, filling of the biliary tract by a barium meal—but in some the diagnosis was confirmed at operation. In most of the cases reported no special symptoms, apart from those due to the duodenal ulcer, could be attributed to the fistula, but sometimes, particularly where the perforation was into the gall-bladder, the symptoms were those of an acute upper abdominal emergency.

CASE REPORT

A company secretary aged 65 developed a few small painless red nodules on his left leg. Biopsy showed these to be due to reticulosarcoma. The nodules cleared up after radiotherapy, but a large ulcer developed at the back of his left knee which never healed. Examination of the peripheral blood showed no abnormality.

Two years later, on November 9, 1952, he was admitted to hospital with marked cachexia, flatulent dyspepsia, and a four-weeks history of painless obstructive jaundice. His faeces were pale and his urine contained bile. His serum bilirubin was 4 mg. per 100 ml. and the direct van den Bergh reaction was positive. Although his general condition deteriorated the jaundice improved dramatically on December 5. He died in coma on December 17, which was almost certainly uraemic.

At necropsy there was no trace of the obstructive jaundice. The pancreas was diffusely permeated by reticulosarcoma, giving the appearance usually associated with a carcinoma of the head of the pancreas (see Fig.). The intrahepatic

and extrahepatic biliary tract above the pancreas was extremely distended. The gall-bladder was distended but contained no stones. In the head of the pancreas the duct cavity was compressed so that the lumen had almost disappeared, and contained no bile. The common hepatic duct communicated with the duodenum through the crater of a large chronic ulcer on the posterior duodenal wall 4 cm. from the pylorus. On histological examination the liver cells contained some bile pigment but there was no dilatation of the perilobular bile ducts or any sign of inflammation around them. Both lobes of the thyroid gland showed nodules of reticulosarcoma, and both kidneys were almost completely replaced by tumour tissue.

COMMENT

In spite of the frequency of duodenal ulcers and their close anatomical proximity to the biliary tract, only very few cases of choledochoduodenal fistula due to perforation of a duodenal ulcer have been found in the literature. Many of these reports are based on radiological evidence only. A case is described in which at necropsy obstructive jaundice was shown to have been relieved by perforation of a duodenal ulcer into the common hepatic duct, thus producing a spontaneous choledochoduodenostomy. No other symptoms could be attributed to the duodenal ulcer or to the perforation. No similar case has been found among those described in the literature.

I am grateful to Professor T. F. Hewer for his help and advice and to Dr. C. D. Evans for the clinical details.

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Reviews

HAEMOLYTIC ANAEMIAS

The Haemolytic Anaemias: Congenital and Acquired. By J. V. Dacie, M.D.(Lond.), M.R.C.P.(Lond.). (Pp. 525+x; 98 illustrations. 50s.) London: J. and A. Churchill, Ltd. 1954.

This book covers a field in which the past few years have seen important advances, and it is fitting that it should come from the pen of one who has already contributed so greatly to our understanding of the subject. It opens with a consideration of the general features of increased blood destruction, and with the methods of investigation of haemolytic anaemia. The next section is concerned with the congenital varieties, and includes excellent and detailed descriptions of elliptocytic haemolytic anaemia, Mediterranean anaemia, and sickle-cell disease. The discussion of the abnormal haemoglobins and their significance is of particular value and interest.

It is not surprising that the sections which deal with acquired haemolytic anaemia of the auto-antibody type should be the most outstanding feature of this book, for it is a subject which Dr. Dacie has made his own, and it is to him that we owe much of our recently acquired knowledge of this form of haemolytic disease. The chapter on the specificity and reactions *in vitro* of the auto-antibodies provides a much needed and invaluable review of this topic.

Later chapters describe the secondary haemolytic anaemias, those of uncertain origin, those due to drugs and infections, paroxysmal nocturnal haemoglobinuria, and haemolytic disease of the newborn. The final section is a useful compilation of the various technical methods required in the investigation of the haemolytic anaemias.

A simple catalogue of its contents shows the all-inclusive scope of this monograph. It covers the subject in a way which has never previously been attempted, and there can be few questions about the haemolytic anaemias to which the answer, if it is known, will not be found between its covers. There is no reason for criticism, if the approach is that of the laboratory worker, for the advances in this subject have sprung from the laboratory, but the clinician will still find in its pages all the help he needs in planning treatment. The author's modest style cannot conceal the authority with which he writes, and every page bears the hall-mark of that personal knowledge and experience which does not merely record but assesses and illuminates the publications of others. Dr. Dacie has placed all those interested in haematology in his debt by providing them, in this model of a scientific monograph, with a greatly needed, comprehensive, and authoritative account of the haemolytic anaemias.

R. BODLEY SCOTT.

DERMATOLOGY

Recent Advances in Dermatology. By W. Noel Goldsmith, M.A., M.D.(Cantab.), F.R.C.P.(Lond.), and Francis F. Hellier, O.B.E., M.A.(Cantab.), M.D., F.R.C.P.(Lond.). Second edition. (Pp. 461+x; illustrated. 42s.) London: J. and A. Churchill, Ltd. 1954.

In 1936 the first edition of this book was completed; its author was W. N. Goldsmith, and few books on dermatology published in the present century have—deservedly—acquired such renown. The second edition is now before us, and it is no less important than the first. It is symptomatic of the times that the present volume has two authors, for, owing to the increasing spate of literature and the ceaseless demands on a consultant's time made by the ancillary tasks which are part of the onus of the Welfare State, it is all but impossible for one man to perform his normal work and contribute significantly to the literature of his specialty. From the reader's viewpoint the collaboration is most fruitful.

The book opens with a chapter on metabolism and passes thence to a consideration of vascular disorders, collagenoses, nervous and psychological matters, endocrinology, vitamins, the affections of reticular tissue, allergy, fungous infections, virus diseases, industrial dermatitis, and radiant energy, with a penultimate chapter on miscellaneous subjects and a final one on therapeutic agents.

The value of the work lies in the careful selection of a great mass of literature and the authors' comments on the papers they have abstracted. This selection and abstraction has required an enormous amount of labour, but there is no evidence of flagging, no smell of the midnight oil, and the vigour of the earlier chapters is maintained to the end. Further, your reviewer has had occasion to check several of the abstracts against the original papers and has been impressed with the great accuracy which has prevailed. To anyone who has never attempted to abstract a paper this may seem a strange remark, but accurate abstracting of all-too-often extremely ill-written papers is a very difficult task, and the authors are to be congratulated on their expertness in this matter.

This is, in fact, a book which all academic and practising dermatologists should "read, mark, learn, and inwardly digest."

R. M. B. MACKENNA.

DISEASES OF THE EYE

May and Worth's Manual of Diseases of the Eye. By T. Keith Lyle, C.B.E., M.A., M.D., M.Chir.(Cantab.), M.R.C.P.(Lond.), F.R.C.S., and A. G. Cross, M.A., M.D.(Cantab.), F.R.C.S. Eleventh edition. (Pp. 724+xii; 305 illustrations and 32 coloured plates. 35s.) London: Baillière, Tindall and Cox. 1954.

The authors have addressed this book to physicians interested in ophthalmology, to undergraduates, and to nurses, and their concise and clear accounts of the common eye diseases and disorders fulfil this purpose admirably. The chapters on squint and the ocular signs of general disease are particularly well done. Although many of the illustrations have been reproduced from previous editions, they are effective; some are new. The book has been enlarged. New chapters have been added on ocular manifestations of injuries and diseases of the central nervous system; on visual field defects due to lesions of the visual tract; the pupils; nystagmus; and ocular neurosis.

Some of the descriptions of operative surgery savour of antiquated techniques; in particular the request to a patient to "look down" instead of using an injection and a bridle suture to produce akinesia of the superior rectus muscle; the dangerous practice of handing the fixation forceps to an assistant to hold the eye down in an iridectomy operation for acute glaucoma; and, indeed, the use of a Graefe knife to make a "section" in this operation instead of the better-controlled *ab externo* operation. A description of Motais's operation for ptosis is dead wood which could be cut from the next edition. Some surgeons who have seen the occasional complication of a divided lateral rectus receding far behind the eye into the posterior part of the orbit would not agree that "free tenotomy of the lateral rectus is quite a sound procedure." The old incision for Krönlein's operation, which produces an ugly scar, is described.

There are several minor faults in proof-correcting: the common site of a scleral rupture is 3 mm. behind the limbus, not 8 mm.; and in the anatomical description of the anterior part of the eye "cavity of aqueous" would be better understood as "anterior chamber."

Much new and valuable information is given about chemotherapy and antibiotics, but no mention is made of

radioactive isotopes in the treatment of retinoblastoma. "Nembutal" is not always a desirable agent for premedication before a local analgesic; under its influence some patients become uncooperative and uncontrollable.

The book is well produced and admirably illustrated, and will be of much value to those for whom it is written. The fact that this is the eleventh edition marks its worth.

H. B. STALLARD.

RATS AND MICE

Control of Rats and Mice. Volumes I and II—*Rats*, edited by Dennis Chitty. Volume III—*House Mice*, edited by H. N. Southern. (Volumes I and II, pp. 532+xxviii+xiii; Volume III, pp. 225+x; illustrated. £5 5s. the set.) London: Oxford University Press. 1954.

Few would have thought that there was sufficient material on this subject to require three substantial volumes to do it justice, but here they are and with a prefatory indication that the work in its present form is about one-third of its original length. We are also told, with admirable candour, that if anyone wishes to get rid of rats it will be cheaper and better to depend on Government bulletins than on these volumes. Acknowledgment is made by one of the contributors to a distinguished scientist for his help and "for a most valuable piece of advice about dealing with Government departments that I had better not repeat here"—a different kind of "Plain Words" perhaps.

This most comprehensive work, the writing of which began in 1946, deals with the extent of rodent infestation, poison baits, properties of poisons, and the response to baits used in rodent control. The habits and behaviour of brown, black, white, ship, and sewer rats—rats urban and rural—are fully considered. The third volume deals with *Mus musculus*—the house mouse. These volumes represent a record of devoted work undertaken over a very long period of years by specialists working in a narrow but important field. They are intended to help those responsible for deciding, on behalf of and in the interests of the public, on methods of rodent control—and this work will be a formidable addition to their weapons.

C. METCALFE BROWN.

THE STRAFFEN TRIAL

Trial of John Thomas Straffen. Notable British Trials Series, Volume 80. Edited by Letitia Fairfield, C.B.E., M.D., and Eric P. Fullbrook. (Pp. 299+xiii; illustrated. 15s.) London: William Hodge and Co. Ltd. 1954.

The editors are to be congratulated on their introduction to this book, in which they give a lucid and readable exposition of the complex legal and medico-legal issues raised by this famous case. All the medical witnesses agreed that Straffen was "feeble-minded" and certifiable as such under the Mental Deficiency Acts, as indeed he had been since the age of 10. He committed his first two murders at the age of 21 when home on licence; he was then found unfit to plead and sent to Broadmoor, but escaped six months later and strangled the third little girl before he was caught within a few hours.

When a defective person is tried for murder and is found fit to plead, as Straffen was in the second trial, the defence plea must be for a verdict of "guilty but insane." Thus Mr. Justice Cassels instructed the jury that they had to consider whether the prisoner was insane within the meaning of the criminal law and not whether he was feeble-minded. Evidence was put before the jury that mental deficiency was quite distinct from insanity and was not a disease of the mind. In his charge to the jury on the M'Naghten Rules the judge pointed out that defect of reason due to disease of the mind had to be proved. In explaining what was meant by the nature and quality of the act, he gave what he described as a very simple illustration (page 244): "If . . . the jury was satisfied that when he strangled that person he thought he was squeezing juice out of an orange, that would be a failure to know the nature and quality of the act." As regards the second "limb" of the M'Naghten Rules, "that means that he did not know it was wrong and that he would have done it even if there had been a couple of policemen looking." In view of the evidence and of these directions there could be only one answer, and the jury returned a verdict of guilty after deliberating for twenty-nine minutes. Straffen was subsequently reprieved after a medical inquiry ordered by the Home Secretary.

As the editors of the book point out (page 25), "Anyone reading the trial of Straffen would find it hard to imagine that mental deficiency was a well-established entity, that intelligence tests are of proved diagnostic value, and that the diminished responsibility of defectives, for every other crime but murder, had been recognized by the law for forty years." The editors also conclude (page 30): "There can be little difference of opinion that the trial of John Thomas Straffen shows the urgent need for a change in the law concerning mentally defective prisoners charged with murder."

All the medical witnesses in this astonishing case were in fundamental agreement. It may be considered that the answers of Dr. Leitch, who as a prison medical officer had Straffen under his care before he was sent to Broadmoor and who was called for the defence in the second trial, did more credit to the medical profession than the questions asked by the Solicitor-General for the prosecution did to the legal profession.

DESMOND CURRAN.

ANAESTHESIA IN GENERAL PRACTICE

Anaesthesia in General Practice. By Stuart C. Cullen, M.D. Fourth edition. (Pp. 312; illustrated. 38s.) Chicago: Year Book Publishers Inc. London: Interscience Publishers Ltd. 1954.

It is very likely that in the future more anaesthetic work in this country will have to be done by general practitioners. There are undoubtedly many such who would like to bring their knowledge of anaesthesia a little more up to date, and Dr. Cullen's book provides an excellent way of reintroducing themselves to the subject. That four editions have been called for in eight years is evidence of its warm reception by general practitioners in the United States. While it treats in an elementary way practically every subject in the field of anaesthesia, the book is naturally not nearly complete enough for examinations like the F.F.A.; the general practitioner studying for the D.A., however, will find the book most useful. A new chapter on ventilation has been included in this edition, while the account of the relaxants has been revised and brought up to date. To lighten the reading some highly entertaining cartoons are included, from which the reader will not only learn some sound common sense but also gain an insight into the current emotional and physical responses to anaesthetic crises in the United States—and into the latest fashion in mortician's accessories.

W. W. MUSHIN.

In *The Captain's Table* (Michael Joseph Ltd., price 10s. 6d. net) Dr. Richard Gordon displays once again the talent for comic descriptive writing that made *Doctor in the House* and *Doctor at Sea* such successful books. The hero is the ingenuous captain of a cargo ship who is suddenly promoted to the command of a crack passenger liner. Between leaving Tilbury and arriving at Fremantle Captain Ebbs undergoes a variety of emotional stresses that would have played havoc with the general adaptation mechanism of a lesser man. The author keeps the story moving quickly from one ludicrous disaster to another, but perhaps shows his best form, as well as a nice sense of parody, in two extracts: the first from the ship's newspaper, edited *faute de mieux* by a junior wireless officer whose enthusiasms do not extend beyond horse-racing, snooker, and the Labour party; and the second from the report of a test match written by an extremely precious cricket correspondent.

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TREATMENT AND PROGNOSIS OF HYPERTENSION

Hypertension with its vascular complications is responsible for a large proportion of deaths over the age of 50, and the management of this disease is one of the chief medical problems of the present time. Usually the cause of the raised blood pressure is unknown, but there is a small number of cases, described by Professor M. L. Rosenheim in his Oliver-Sharpey lectures (published in last week's *Journal*), where a cause can be found and treatment may result in cure. Unilateral renal disease, often due to pyelonephritis, is the commonest cause of these, and nephrectomy may result in cure of the hypertension. A phaeochromocytoma, the functioning tumour of the adrenal medulla, may cause either sustained or paroxysmal hypertension, and the use of phentolamine (" rogitine "), which antagonizes the peripheral action of the circulating amines, or the estimation of the pressor amines in the urine, may enable the diagnosis to be confirmed. The cases in which a cause for the hypertension can be found are admittedly rare, but since treatment often results in cure, with disappearance of the secondary vascular complications, they should always be borne in mind, particularly when there is no family history of hypertension or if the patient is young, when severe hypertension is nearly always secondary.[1]

Unfortunately in most patients no cause for the hypertension can be found, and treatment is necessarily empirical or symptomatic. However, if the blood pressure can be lowered appreciably by either surgical or medical treatment the progressive or malignant phase of hypertension, whether essential or renal in origin, may be converted into the benign one, with retrogression of the retinal changes and improvement in the electrocardiogram.[2 3] The methonium compounds are the most effective drugs at present available for lowering blood pressure, and the papers by Professor Rosenheim, Dr. Shirley Smith and his colleagues (in the opening pages of this week's *Journal*), and Drs. Graham and Maxwell (p. 1250) all confirm earlier reports[4] of both subjective and objective improvement in patients with severe or malignant hypertension. A satisfactory reduction in blood pressure by hexamethonium can be obtained only if the drug is given subcutaneously, and three injections a day are necessary for adequate control. Hexamethonium given by mouth often relieves symptoms, but it has no place in the treatment of severe hypertension, for which lowering of blood pressure is the urgent consideration. Pentapyrrolidinium (" ansolysen "), another ganglion-blocking drug, is sometimes effective by mouth, and with the smaller dose necessary side-effects are less frequent. Among the many other drugs which are at present having a vogue are preparations of veratrum, hydralazine (" apresoline "), and rauwolfia. These are thought to act centrally on the hypothalamus and have the advantage of being given by mouth. They are not entirely free from side-effects, and since their hypotensive action is mild they are commonly prescribed in combination with other hypotensive drugs.

The difficulties of hexamethonium treatment are emphasized in all these recent papers, and it is clear that this is a treatment which is difficult for both doctor and patient if it is to achieve the desired lowering of the blood pressure. Like the rice diet and the low sodium diet, which if persevered with will produce the same improvement in the manifestations of hypertension, hexamethonium treatment is often abandoned by the patient after the first few months, either because of unwillingness to carry on the necessary injections or because the side-effects are more troublesome than the symptoms of the disease. For this reason there is a return of interest in the surgical treatment of hypertension, which has to a large extent been replaced by medical treatment in recent years. Despite the well-recognized tendency of the blood pressure to return to the pre-operative level many authors report an increase in the survival rate after operation,[3 5] and Kahn,[6] in a recent review, concluded: " It is regretted that a procedure that has been proved by highly competent surgeons to improve life expectancy in severely ill hypertensive patients has not been accepted by the majority of practising physicians."

The decision on when an attempt should be made to lower the blood pressure is a difficult one, for the prognosis for the individual with hypertension is often

[1] Platt, R., *Quart. J. Med.*, 1948, **17**, 83.
[2] Smirk, F. H., *British Medical Journal*, 1954, **1**, 717.
[3] Morrissey, D. M., *et al.*, *Lancet*, 1953, **1**, 403.
[4] Morrison, B., *British Medical Journal*, 1953, **1**, 1291.
[5] White, P. D., *et al.*, *J. Amer. med. Ass.*, 1950, **143**, 1311.
[6] *New Engl. J. Med.*, 1954, **251**, 633.
[7] Bechgaard, P., *Acta med. scand.*, 1946, Supplement 172.
[8] *J. Amer. med. Ass.*, 1953, **153**, 1.
[9] Sokolow, M., *et al.*, *Ann. intern. Med.*, 1953, **38**, 647.
[10] Leishman, A. W. D., *British Medical Journal*, 1953, **1**, 1131.
[11] *Lancet*, 1953, **1**, 1261.
[12] Allen, E. V., *et al.*, *Proc. Mayo Clin.*, 1954, **29**, 459.

difficult to assess. Essential hypertension is a progressive disease, but in the majority of cases, especially if there is no evidence—either clinical or cardiographic—of myocardial damage, the rate of progress is slow.[7] On the other hand, the disease sometimes runs an "accelerated" course, and Palmer and Muench[8] found that only 11% of their patients with secondary changes in the heart, kidneys, or brain were alive after ten years. The prognosis in malignant hypertension — characterized clinically by papilloedema and a diastolic pressure usually over 130 mm. Hg and pathologically by the presence of acute arteriolar necrosis—is bad, the average survival from the time of recognition of the papilloedema being only about eight months.[9] The indications for drastic treatment are clear in malignant hypertension, since there is definite evidence of improvement in survival rate after either medical treatment with ganglion-blocking drugs or surgical sympathectomy. The presence of advanced retinal changes, albuminuria in excess of a trace, and cardiac enlargement or abnormality of the electrocardiogram indicate that the disease is likely to run an accelerated course,[10] and the authors of the reports in this issue have found that the immediate results of drug treatment are good. It is too soon to know whether the distant prognosis is improved, but it seems likely that it will be if the patient and doctor are prepared to carry on with treatment indefinitely.

Neither the actual level of the blood pressure, provided the diastolic pressure is under 130 mm. Hg, nor the presence of so-called hypertensive symptoms such as headache and fatigue—which Stewart[11] showed to be often due to anxiety—should influence the decision to start treatment with hexamethonium. Patients with moderate hypertension are probably best left alone or, if symptoms are present, treated with the centrally acting drugs such as rauwolfia. In these milder cases it would seem to be quite unreasonable to embark on an endless course of treatment which according to some authorities involves the patient in obtaining a sphygmomanometer and taking his blood pressure seven times daily.[12] Dr. Shirley Smith and his colleagues stress that if a treatment of hypertension is to be acceptable then general practitioners must be able to undertake it while their parents live at home and pursue their daily work. It is doubtful whether according to these criteria hexamethonium is an acceptable treatment for any but the most severe cases of hypertension. For patients without vascular complications measures such as weight reduction and the use of simple sedation are probably all that are needed, with, if symptoms are prominent, a trial of drugs such as the veratrum or rauwolfia preparations.

DANGERS OF ACUTE RESPIRATORY INFECTION

Chronic bronchitis is unfortunately often regarded lightly by patient and doctor alike until the advent of crippling and sometimes fatal complications emphasizes the serious nature of the disorder. Earlier this year we drew attention to the rapid deterioration in patients with chronic bronchitis and emphysema when an acute respiratory infection supervenes.[1] These patients become quickly cyanosed, pass into right heart failure, and develop mental confusion which sometimes precedes coma and death.[2] Exacerbations of respiratory infections usually occur in the winter months,[3] and it is now abundantly clear that such infections account for the heavy mortality in sufferers from pulmonary diseases who have to breathe polluted air in the form of "smog." General practitioners having under their care bronchitic patients who approach the coming winter with apprehension will find that the paper by Dr. E. K. Westlake[4] in a recent *Journal* gives some insight into the mechanism of the breakdown in these patients and some guidance for their treatment. Westlake's studies of the arterial blood gases and *p*H have emphasized the importance of respiratory failure as the cause of the sickness and death during exacerbations of bronchitis. He defines respiratory failure as the breakdown in the normal function of the respiratory centre in response to carbon dioxide retention and anoxia, which in a normal subject leads to hyperventilation and the restoration of gaseous equilibrium. Many patients with chronic bronchitis and emphysema are already in a state of chronic respiratory failure with moderate anoxia and hypercapnoea. Intercurrent lung infections in such patients will precipitate acute respiratory failure, since the additional stimuli of pyrexia and anoxia fail to produce sufficient hyperventilation to prevent further increase in the carbon-dioxide tension in the blood. The chemical changes of respiratory failure are directly responsible for many of the well-recognized clinical manifestations seen during respiratory infections in bronchitic patients. Anoxaemia, hypercapnoea, and acidaemia give rise to cerebral vasodilatation and are the cause of such symptoms and signs as headache, papilloedema, sweating, mental confusion, coma, and myoclonic twitching.

[1] *British Medical Journal*, 1954, **1**, 322.
[2] Simpson, T., ibid., 1954, **1**, 297.
[3] Oswald, N. C., Harold, J. T., and Martin, W. J., *Lancet*, 1953, **2**, 639.
[4] *British Medical Journal*, 1954, **2**, 1012.
[5] Roettig, L. C., Reiser, H. G., Habeeb, W., and Mark, L., *Dis. Chest*, 1952, **21**, 245.
[6] Ungar, L., and Ungar, A. H., *J. Amer. med. Ass.*, 1953, **152**, 1109.
[7] Miller, J. B., and Boyer, E. H., *J. Pediat.*, 1952, **40**, 767.
[8] Halm, W. H., May, J. R., and Livingstone, J. L., *Lancet*, 1954, **2**, 630.
[9] Ibid., 1954, **2**, 51.
[10] *British Medical Journal*, 1954, **2**, 1018.

The practical importance of Westlake's findings is that they provide a logical basis for the treatment of patients suffering from respiratory failure due to an acute exacerbation of an infection. It is of paramount importance to give patients antibacterial treatment to relieve anoxia and to free the respiratory passages from obstruction. Penicillin in the usual dosage does not eliminate the infection with *H. influenzae* which is so common in bronchitis; streptomycin or one of the tetracyclines are more effective. Although the relief of anoxia is an essential part of treatment it should be undertaken with an appreciation of the risks entailed, since abolition of anoxia diminishes the only efficient remaining stimulus to respiration. Sudden relief of anoxia may therefore lead to depression of the respiratory centre, with further carbon dioxide retention and consequent confusion, twitching, and coma. Oxygen should be given slowly at first—at a rate certainly not exceeding three litres per minute. Similarly, morphine and other depressant drugs should be avoided, since they will also aggravate respiratory failure and may even hasten death. Bronchospasm should be relieved by the usual bronchodilators and, if these fail, by corticotrophin or cortisone. Postural drainage and coughing should be encouraged to free the air passages, but mechanical artificial ventilation has not proved helpful. Some success has recently been reported from the use of purified trypsin or synthetic detergents administered by aerosol mists in clearing the respiratory passages of tenacious sputum[5 6 7]: further experience may show that there is a place for such therapy. Prolonged antibiotic treatment, which has been used with encouraging results in the treatment of chronic bronchitis,[8] may also be valuable in the prevention of respiratory breakdown during the winter months.

Failure of the right side of the heart is an additional hazard to which patients with chronic bronchitis are exposed. Cor pulmonale, once a rare cause of heart failure, was found by Flint[9] to be the commonest single cause of congestive failure in patients admitted to a general hospital. Acute respiratory infection often precipitates heart failure, since infection and anoxia cause an increase in pulmonary pressure with consequent additional strain on the already overtaxed right ventricle. Heart failure, though not often a direct cause of death in chronic bronchitis, nevertheless calls for urgent treatment when it is a complication of respiratory infection. Flint[10] has also shown that acute respiratory infection is a cause of congestive failure not only in cor pulmonale but also in patients with rheumatic hypertensive and ischaemic heart disease. In these patients the mechanism of the heart failure is not fully understood, but it is a matter of practical importance that they will often recover more rapidly if antibiotics are given in addition to the usual treatment of congestive failure. Even so, as Dr. H. Joules emphasizes this week (p. 1259), the lesson has still to be learnt that much chest disease is preventable: "Our community and our profession are dying needlessly."

PERINATAL DEATH RATE

Last year the infant mortality rate in England and Wales reached the record low level of 27 per thousand live births. For boys it was 29.9 and for girls 23.6. In comparison with the last pre-war year, 1938, when it was 53, the rate has therefore been just about halved. Recording these and other indices of the nation's health in 1953, the Chief Medical Officer of the Ministry of Health, Sir John Charles,[1] gives emphasis once again to the fact that the infant mortality rate has come to have two quite diverse components. These are respectively the death rate for the first four weeks of life, or the neonatal death rate, and the death rate for the remaining eleven months of the first year, or the postnatal (or post-neonatal) death rate. While the overcoming of infectious diseases that has been so notable a feature of the last twenty years has enabled the postnatal death rate to contribute a drastic reduction to the infant mortality rate, the deaths in the first four weeks of life are not so much caused by these now more easily controlled diseases as by prematurity, birth injury, congenital malformations and so on. The death rate from these is still falling year by year, but at a much slower pace. They contribute, too, a much higher proportion of the infant mortality rate than they used to do, and in consequence this rate is unlikely to be such a sensitive indicator of social conditions as formerly.

A curious feature of the infant mortality rate, reduced as it has been over the years, is that the disparity between the social classes remains much as it has always been. The rate in 1921 for legitimate infants in class I was 38.4 and in class V 97.0, or 2.5 times as high. In 1950 the class I rate was 17.9 and the class V rate 40.7, or 2.3 times as high.[2] In 1921 the class V neonatal rate was 1.6 times the class I rate; in 1950 it had slightly worsened to 1.7 times the class I rate. The postnatal rate of class V in 1921 was 4.0 times the class I rate, and in 1950 it had slightly improved to 3.8 times this rate. It is certainly surprising that the tremendous social changes of the last

[1] *Report of the Ministry of Health for the year ended December 31, 1953, Part II On the State of the Public Health*, 1954, H.M.S.O., London.
[2] *The Registrar General's Decennial Supplement, England and Wales, 1951, Occupational Mortality, Part I*, 1954, H.M.S.O., London.

thirty years should have benefited all so equally, and the hopeful inference may possibly be drawn that we are far yet from a flattening out in the curve of infant mortality, for some closure of the gap may be expected from these changes in due course.

If some separation is generally to be made in future between neonatal and postnatal mortality, there is much to be said for grouping these deaths rather differently than before and after the four-weeks point. Whether a baby dies just before, during, or after birth is sometimes a matter of chance, and possibly of speculation; the causes of stillbirths are often the same as those of early neonatal deaths. Consequently Sir John Charles and Dr. W. P. D. Logan (of the General Register Office) canvass in this report the idea of the perinatal death rate. It would be calculated from the stillbirths combined with the deaths in either the first week or some other interval of life. The most medically significant interval should not be too difficult to agree upon. We should then have two new rates to consider—namely, the perinatal and the rate for the rest of the first year of life—in place of three old rates—the stillbirth, neonatal, and postnatal.

TUBERCULIN TESTS

Tuberculin skin tests are capable of yielding much valuable information when used as quantitative measures of tuberculin sensitivity. For the most part, however, they are used only qualitatively to detect the presence of infection by tubercle bacilli. As none of the tests gives completely specific reactions it is necessary to have arbitrary definitions of "positive" and "negative." The tuberculin jelly test has been used for nearly twenty years and many decisions and conclusions must have been based on its results, but there is still no agreement on the criteria for a "positive" reaction. Before the tuberculin survey[1] by the Medical Research Council was started the accuracy of the jelly test was re-examined.[2] A positive result was then defined as "an area of raised erythema with or without vesiculation at the site of the test." Although this was adopted for the survey, the description of the preliminary investigations gives a different criterion, "four or more vesicles" being necessary. Any test depending on one pimple more or less is immediately suspect. Light abrasion of the skin with fine sandpaper (flourpaper) was used to increase the sensitivity of the test. It appears to have done so; but it also increased the number of doubtful and inaccurate results.[3,4]

Caplin and his colleagues at the London Chest Hospital and Highwood Hospital for Children have recently investigated the flourpaper test very thoroughly, and their results were reported in this *Journal*.[5] They began by examining the skin lesions produced by the plain jelly test. None of the children negative by the usual criteria to the intradermal injection of 100 tuberculin units (T.U.) of old tuberculin (O.T.) showed a reaction to the jelly test after 72 hours. When the flourpaper technique was used the reactions in both Mantoux positive and negative children were much more violent. The number judged to be infected varied according to the method used and standard adopted. Thus, in a group of 288 children the Mantoux test gave 115 positive, but only 76 by the flourpaper jelly test read according to the standard accepted in the M.R.C. survey. By another commonly used standard the number was also 115; but not all these children were judged positive by the Mantoux test. Caplin and his colleagues then investigated the accuracy with which the reaction could be read. Four observers relatively inexperienced in such work read both the Mantoux and the flourpaper tests. All agreed in 96% of Mantoux tests read at 96 hours, but in only 20% of jelly tests. Two observers with much more experience agreed in only 63% of 437 tests. The same children had a Mantoux test (10 T.U.) read by another experienced pair at the same time: they agreed in 99.8% of the tests. The observers using the Mantoux test judged 17% to be positive, while one observer using the flourpaper jelly test recorded 21% positive and the other 43%, which included 34% of those judged negative by the Mantoux test.

It is generally agreed that the intradermal method is a more accurate indication of tuberculous infection. It seems that the flourpaper jelly test is not only grossly inaccurate in comparison but also allows of much greater variation between observers. Caplin and his colleagues conclude that its inaccuracy "precludes its use both in clinical practice and in tuberculin surveys." This statement is amply justified, and no survey based on the test can be accepted. The plain jelly test is less objectionable and a "positive" result can probably be relied on in clinical practice. A negative result, however, must be confirmed by an intradermal test. The jelly test is probably useful only in screening very young child contacts of tuberculous patients. The Heaf multiple-puncture test[6] has not been fully investigated and cannot yet be adopted, though two encouraging reports appear in our correspondence columns this week (p. 1292). The Mantoux test still remains the most reliable; and the Expert Committee on Tuberculosis of the World Health Organization recently recommended[7] that a single Mantoux test with 5 T.U. should be used for mass vaccination.

A LUSTY TWO-YEAR-OLD

A gavel made from the wood of an ancient plane tree from the Isle of Cos lately called together the College of General Practitioners for its second annual meeting (see p. 1282). The College is a lusty two-year-old. It has been cradled in general good will. Eschewing medical politics, it has been in contact with many organizations but in collision with none. The second annual report,

[1] *Lancet*, 1952, 1, 775
[2] Dick, W. P., *British Medical Journal* 1950, 2, 141.
[3] Coles, H. M. T., *Lancet*, 1952, 2, 927.
[4] Frew, H. W. O., Davidson, J. R., and Reid, J. T. W. *Brit. J. Tuberc.*, 1953, 47, 68.
[5] *British Medical Journal*, 1954, 2, 895.
[6] Heaf, F., *Lancet*, 1951, 2, 151.
[7] *Wld Hlth Org. techn. Rep. Ser.*, No. 88, October, 1954.

just published from 14, Black Friars Lane, E.C.4, speaks of happy relations with innumerable bodies—the Ministry of Health, the medical schools, the World Health Organization, and so on; of the British Medical Association the report says that "every department . . . with which the College has come into contact has been most helpful and encouraging."

A general increase in size and activities is recorded. The total number of members at the end of September last was 2,967, of whom 345 were overseas. The report discusses possible criteria for membership in some detail and comes down, at any rate at present, against an examination. Nevertheless membership of the College "should indicate a practitioner of mature and balanced judgment," and the council has taken great pains to define the standards required for membership in the future. While it is recommended that candidates for full membership should, among other requirements, have been qualified for at least seven years, associate membership will be open to all registered or provisionally registered medical practitioners. The present year has seen the foundation of the last 12 regional faculties in the British Isles, making 22 in all, with five more in other parts of the Commonwealth. Each of these faculties represents the College in its area and has identical aims and objects. Their duty is to relieve the College council of local responsibilities connected with the activities of the College in the regions concerned. The Undergraduate Education Committee of the College is finding its main task the collection of information from the College faculties and the sharing out of results within the general membership. The committee has also addressed itself to the subject of the medical curriculum and has ascertained the opinion of the faculties, all of which feel that more detailed attention ought to be given to certain branches of medicine and in particular to the commoner diseases. Many of the faculties feel that the student should be taught to realize better the very wide field covered by general practice, and to recognize how much of medicine lies within the realm of the family doctor. The Postgraduate Education Committee has undertaken a survey of the arrangements already existing for the postgraduate education of general practitioners throughout the British Isles, and in its report has a good deal to say on the planning of postgraduate courses. Yet another committee is charged with research in general practice. On this point the committee says that the potential for further development in general-practitioner research is present, and in time, when circumstances are favourable, full use will be made of it. In the meantime a number of College- and faculty-sponsored investigations are in hand, and several study groups have been formed; the College has been gratified by the number of practitioners who are willing to take part in its investigations. As for plans ahead for the College, it is hoped soon to install a department for helping general practitioners in the planning of their surgeries and in alterations to their premises.

Since last year a Scottish council has been constituted, with Dr. J. M. Henderson, of Pitlochry, as its chairman, and cordial relationships have been established with the Royal Colleges in Edinburgh. In Scotland also committees on undergraduate and postgraduate education have been constituted. The question of morbidity surveys has been considered at length by the Research Committee of the Scottish Council, but members have been advised to concentrate on investigations involving comparatively little record-keeping by the doctor and to select short-term investigations and those which are likely to yield useful results in the early future.

EPSOM COLLEGE CENTENARY APPEAL

In 1855 what was then called the Royal Medical Benevolent College was opened at Epsom by the Prince Consort, who had been prevented from laying the foundation stone two years before by an attack of measles. The idea of the college was conceived by Mr. John Probert, a member of the council of the Provincial Medical and Surgical Association (the forerunner of the British Medical Association), who said, when speaking at the lunch which followed the opening ceremony: "I hope and trust our building will endure and be a blessing to generations yet to come. But let me intreat you to bear in mind that the expenses will be considerable, and I trust you will continue to stir up your friends in its behalf." Mr. Probert's hope has been more than fulfilled, for Epsom College is now a well-known public school, and it is by no means only in the medical profession that distinguished Old Epsomians will be found. But the need for financial support, which Mr. Probert foresaw, is as great as ever, if not greater. Like other public schools, Epsom is finding the cost of modernizing its buildings beyond its financial resources, and a centenary appeal has just been issued so that the school can "embark with confidence on a second hundred years of vigorous life and useful service to the community." The appeal, signed among others by Lord Webb-Johnson, the president of the Royal Medical Foundation of Epsom College, is addressed to all who have cause "to wish College and Foundation well, who are interested in seeing a good independent school survive without lowering standards, and who recognize that without a substantial contribution from her friends that survival is unlikely."

Through its foundation Epsom has a closer link with the medical profession than any other public school. About one-third of the 6,500 boys who have been educated there have become doctors, of whom a great many have been assisted financially or in others ways by the College or Foundation. In one hundred years there have been 800 Foundation Scholars, educated, maintained, and clothed free of charge by the Foundation, and in a recent year 100 out of 352 boarders were receiving help from one College source or another. In addition to 25 leaving scholarships available for boys studying medicine, nine London teaching hospitals award scholarships to Epsomians every year. Thus, besides encouraging the intellectually talented, Epsom is able to help in the best possible way the sons of many medical men who for one reason or another might have been deprived of a

first-class education. The council of the College is aiming to raise not less than £150,000, and the medical profession will surely wish to support an appeal for such a worthy cause.

INTRAMUSCULAR IRON THERAPY

Some patients suffering from hypochromic anaemia are either refractory to all forms of oral iron medication, owing to limitations of alimentary absorption, or cannot take it because of severe gastro-intestinal disturbance. Since Nissim[1] published his notable paper on the treatment of hypochromic anaemia with intravenous iron injections, it has been possible to treat these people successfully by this method. Intravenous iron medication has certain drawbacks. There may not be any visible or palpable veins suitable for giving an injection. The injections must be given by a medical practitioner, and, if not administered skilfully, leakage into the surrounding tissues produces severe local pain, swelling, and staining of the skin. However carefully the iron is given, venous thrombosis with permanent occlusion of the vein is a frequent complication. Unpleasant allergic reactions, with a few deaths, have been reported following intravenous iron therapy. A safe intramuscular iron preparation which would avoid some of these difficulties has long been required. Intramuscular iron injections have been given by various workers,[2–5] but hitherto these solutions, especially injectio ferri of the *British Pharmacopoeia*, have been so toxic that only small, virtually useless amounts have been tolerated.

Now the results of two clinical trials with a carbohydrate iron preparation ("imferon") for intramuscular use are reported in the *Journal* this week at pp. 1255 and 1257. Professor D. F. Cappell and his colleagues at Glasgow gave this substance to fifteen patients suffering from iron-deficiency anaemia who were refractory to, or intolerant of, ferrous sulphate orally, and Drs. J. M. Scott and A. D. Telford Govan administered it to fifty pregnant women with iron-deficiency anaemia. Both these teams of workers obtained satisfactory absorption and utilization of the iron without any serious systemic reactions. Although there was a satisfactory rise in the haemoglobin concentration, the serum iron peaks varied considerably, and this may indicate that the iron is not always entirely satisfactorily absorbed from the site of the injection. The dose schedule is still under consideration, but it appears that it will be in the neighbourhood of 200 mg., or 4 ml., every other day or twice a week. Baird and Podmore[6] have reported that thirty-eight out of forty cases of iron-deficiency anaemia responded adequately when given imferon in similar doses. All these workers report slight local tenderness and discomfort at the site of the injection, but no more than would be expected from any other intramuscular injection. Sometimes local staining of the skin results.

Although no systemic allergic reactions developed in the series under review, this hazard always remains when a heavy metal is given either intramuscularly or intravenously. It is therefore too early yet to advocate that the uncomplicated iron-deficiency anaemia so often seen in pregnancy should be treated by iron intramuscularly. Extensive clinical trials with this intramuscular preparation over prolonged periods are needed to exclude the possibility of late allergic reactions before such a course should be contemplated. Intramuscular iron therapy seems likely to be useful particularly in the treatment of those patients suffering from refractory iron-deficiency anaemia, and those who are intolerant to oral iron or who have reacted unfavourably to intravenous iron injections. It is not known yet whether hypochromic anaemia secondary to chronic infections, such as rheumatoid arthritis, will respond to iron given intramuscularly.

MEASURING MORBIDITY

In order to give greater precision to investigations into morbidity as distinct from mortality the General Register Office asked a committee of distinguished medical practitioners and statisticians to prepare definitions of the rates and other measurements likely to be used. Their report has now appeared[1]; it should be a useful and influential publication. The collecting and analysis of morbidity statistics, except for those of infectious diseases, is still in its first youth, and the quantities measured differ in many respects from those so familiar in mortality statistics. Patients fall ill and recover, for instance, remaining ill for a time between these two events. Three quantities thus emerge immediately to provide such rates as the number falling ill in a given time, the number who are ill in a given time, the number of spells of sickness starting in a given time (which may be much more than the number of people starting them), and so on. Though simple enough in themselves, such rates as these have only in recent years attained much prominence, chiefly as a result of the extension of medical inquiry into the many everyday illnesses that contribute little to mortality statistics but much to human suffering, inefficiency, and penury.

The peculiarly English word "spell," which is of uncertain etymology, figures largely in these definitions, with the ordinary meaning that it bears in the phrase "spell of illness." As an example of one of the definitions the following may be quoted; it describes the average duration of sickness per completed spell of sickness: "The total of the entire duration of all spells of sickness ending during a defined period divided by the number of spells ending during that period." The short title of this measure is given as "average duration per spell." Like most definitions, these are rather forbidding as reading matter, but as tools for research workers they should be invaluable. General practitioners carrying out investigations in their practices would find this pamphlet particularly useful.

[1] Nissim, J. A., *British Medical Journal*, 1954, **1**, 352.
[2] Barlow, W. J., and Cunningham, R. L., *J. Amer. med. Ass.*, 1911, **67**, 1435.
[3] Bullock, E. S., and Peters, L. S., ibid., 1911, **57**, 1428.
[4] Heath, C. W., Strauss, M. B., and Castle, W. B., *J. clin. Invest.*, 1932, **11**, 1293.
[5] Stockman, R., *British Medical Journal*, 1893, **1**, 881, 942.
[6] Baird, McLean I., and Podmore, D. A., *Lancet*, 1954, **2**, 942.

[1] *Studies on Medical and Population Subjects, No. 8. Measurement of Morbidity*, 1954. H.M.S.O. 1s. 6d.

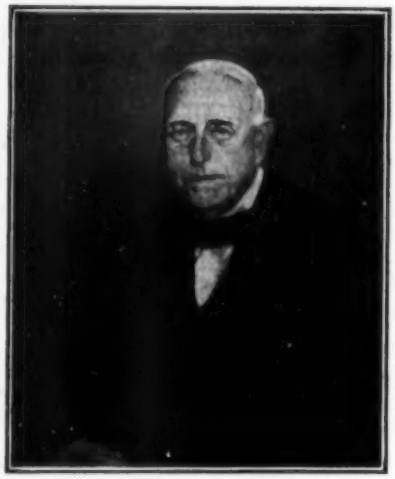
THE COLLEGE OF GENERAL PRACTITIONERS

FIRST JAMES MACKENZIE LECTURE

When the College of General Practitioners was founded two years ago, *The Practitioner* presented to it an annual lectureship in honour of the memory of James Mackenzie. The first of these lectures was delivered in London on November 20 by Dr. WILLIAM N. PICKLES, the first president of the College, before a large audience which filled the Great Hall at B.M.A. House.

Epidemiology in Country Practice

Taking as his subject "Epidemiology in Country Practice," Dr. Pickles began with a quotation from Jane Austen on how to write a book: "You must employ the material which lies closest to your hand; you must contrive your story out of the simplest every-day matters, as a small bird builds its nest from the mosses and twigs of the tree it lives in"; and he ended with another from T. H. Huxley: "Sit down before fact as a little child; be prepared to give up every preconceived notion: follow humbly and blindly wherever nature leads or you shall learn nothing." Between these two quotations, Dr. Pickles drew on his rich experience of epidemic disease in Wensleydale. He recalled his perplexity at the recurrence of epidemics of jaundice, and was puzzled to know whether what he was seeing was a mild form of Weil's disease. Probing ceaselessly for the source of infection, he concluded in 1929 that the incubation period of epidemic jaundice was about a month, the period of infectiousness about a week, and that the disease was spread from person to person by droplet infection. By means of charts he was able to show that a girl at a village fête transmitted the disease to 13 other people.



Dr. W. N. Pickles, first President of the College of General Practitioners.

Next he described how a schoolmistress with influenza, by attending school for a brief morning session, spread the infection to 78 persons among her pupils and their families. Later he was able to show that in a village some degree of immunity, lasting between four and seven years, followed an influenza epidemic. By a similar technique, the second and third waves of measles, from a single source, were clearly demonstrated at approximately twelve-day intervals, and also a relationship between chicken-pox and shingles. In his records of 20 years, more than 6,800 instances of infectious disease had been tabulated, diarrhoea and vomiting being closely followed by influenza as the commonest, with diphtheria and poliomyelitis the least frequent.

Dr. Pickles then proceeded to give a graphic account of the first case of Bornholm disease to be recognized in this country—"a disease of alarming symptoms but no death rate." Though well aware that the only possible danger was that patients with this disease might fall into the hands of a surgeon, to the delight of his audience he admitted that he had fallen into the trap himself. "If only I had been able to wait another day, the development of retrocaecal appendicitis in four other members of the family . . ."

In conclusion, Dr. Pickles recalled that when he was Lord Moynihan's dresser James Mackenzie came in to watch an operation; and much later he was to learn that Mackenzie had ushered into the world the baby who became Mrs. Pickles.

In proposing a vote of thanks, Dr. JOHN HUNT paid a warm tribute to Dr. Pickles, which was received with acclamation. "Of all the characteristics which Dr. Pickles shared with James Mackenzie, it was his inquisitiveness and curiosity which had led to his greatest work." No doctor, Dr. Hunt went on, was so busy that he could not take a special interest in some matter where the growing points of medicine impinge on general practice; and they nearly all did somewhere, somehow. Instead of adding to a doctor's burden, such an interest might give zest to his work and might even prove to be a relaxation in the routine of the daily round. It was through the encouragement of such curiosity in its members and associates that the College of General Practitioners, in time, might make its greatest contribution to the medical services of this country.

SECOND ANNUAL GENERAL MEETING

Later in the day, in the same Hall, generously lent for the occasion by the British Medical Association, more than 300 members and associates attended the second annual general meeting of the College. The chairman of council, Dr. G. F. ABERCROMBIE, in presenting the Annual Report congratulated the President on the reproduction of his portrait (shown on this page) which forms the frontispiece, and expressed the thanks of those present for all he had done for the College during his year of office.

The Year's Progress

After referring to the work of the Undergraduate and Postgraduate Education Committees, Dr. Abercrombie turned to the research programme. The College Register, which last year contained about 50 names, now stood at nearly 400. In consequence a very considerable expansion of the research committee was required, and it was intended to appoint, in addition to the officers now serving on it, an honorary secretary, an honorary assistant secretary, a registrar, an editor of newsletters, and later a treasurer of the research fund which had just been opened. The plan for the National Morbidity Survey was complete and there would be a rehearsal of the whole team—about 120—next year. "If this College never does anything else," he said, "it will still have contributed notably to British medicine by stimulating the interest and co-ordinating the efforts of hundreds of general practitioners in the field of clinical research."

The year had seen the foundation of the last 12 Regional Faculties in the British Isles, making 22 in all, and there were five faculties overseas. Messages of greeting on this occasion had been received from the New South Wales faculty in Australia and the Auckland faculty in New Zealand.

On the subject of criteria for associateship and membership—criteria for fellowship were not yet under discussion—Dr. Abercrombie said the question whether an examination should form part of the criteria for entry, or not, was the greatest immediate problem before the College. The first council had decided against an examination as a criterion for membership at present, but had authorized the formation of a committee to study the technique and detail of such an examination if, in the future, it should be decided to introduce one.

The financial report and balance sheet showed that the College had about £20,000 invested, and it was intended to preserve this sum untouched. Council recommended that associates should pay an annual subscription of one guinea but no entrance fee, and that members should pay an annual subscription of three guineas in addition to the entrance fee of ten guineas. If these recommendations were accepted the College would be paying its way.

After a graceful tribute to the work of the honorary secretary, Dr. John Hunt, the Chairman reminded his

audience that two years ago the College did not exist. Today it had a president and more than 3,000 members and associates. "Let us go on then," he said, "in the path—academic and not political—which we have deliberately chosen. If anyone who contemplates joining us should ask of you 'What benefit will membership confer?' say this: 'First, you will receive a copy of the annual report; next, you will be introduced to a Faculty. Through these two agencies, you will find yourself in close touch with something new and good in the general practice of the day and of the future; and, if you wish, you may take your share in this enterprise with those whose courage and vision have created a living thing from a dream a hundred years old."

The adoption of the annual report, together with the accounts and the report of the auditor thereon, was seconded by the treasurer, Dr. H. L. GLYN HUGHES, and carried unanimously.

Elections and Presentations

Dr. IAN GRANT then proposed, and Dr. CHARLOTTE NAISH seconded, that Dr. W. N. Pickles be re-elected President of the College for 1954–5. There being no other nominations, the CHAIRMAN declared him elected. As Dr. PICKLES made acknowledgment the whole audience rose and greeted him with an ovation which must indeed have warmed his heart.

The PRESIDENT then received from Dr. ANNIS GILLIE, representing the Medical Women's Federation, a very beautiful visitors-book, inscribed in memory of Dr. Christine Murrell, who did so much for the status and welfare of general practitioners. A second presentation was made by Dr. R. A. MURRAY SCOTT, on behalf of the Yorkshire Faculty, of a portrait of Dr. Pickles. This fine portrait, by Mr. Christopher Sanders, A.R.A., had been on view in the morning before the James Mackenzie lecture, and was declared on all sides to be an excellent likeness.

Thirty-five names had been proposed for the College Council. A motion from the floor that the council this year be enlarged if necessary to 45 members was carried; and, as no ballot was required, the CHAIRMAN declared the 35 nominees elected. The names of these and their faculties are as follows:

G. F. Abercrombie (London North), G. O. Barber (Northern Home Counties), T. R. Bryant (Wales), F. S. Catto (North-west England), K. McL. Cobban (Merseyside), D. L. Crombie (Midland), K. M. Foster (North Midlands), W. S. Gardner (West Scotland), W. W. Gerrard (South-east England), Annis C. Gillie (London West), F. J. Goddard (London East), St. G. B. Delisle Gray (Northern Home Counties), Robert Harkness (North-east England), J. M. Henderson (East Scotland), W. V. Howells (Wales), H. L. Glyn Hughes (London South), J. H. Hunt (London South), J. M. Hunter (Northern Ireland), David Kyle (Wales), J. P. J. Little (West Ireland), R. M. S. McConaghey (South-west England), K. A. Mackay (North Scotland), Laurence Masterson (East Ireland), Charlotte Naish (North-east England), J. G. Ollerenshaw (Yorkshire), R. J. F. H. Pinsent (Midland), F. M. Rose (North-west England), J. C. T. Sanctuary (Northern Home Counties), Richard Scott (South-east Scotland), R. A. Murray Scott (Yorkshire), George Swift (South-east England), W. G. Tait (Thames Valley), C. A. H. Watts (Midland), G. I. Watson (South-east England), and J. Campbell Young (Northern Ireland).

Constitutional Changes

Dr. F. M. ROSE proposed a special resolution to alter the Articles of Association in such a way that from 1955 onwards each faculty would elect its own representative on council. The College would, however, retain the power to appoint at a general meeting a number of members of council; and the College council, in special circumstances, might itself make appointments. This resolution was carried unanimously.

Among the College by-laws which were agreed were the following:

Criteria for Associateship: A person shall be eligible for admission as an associate if he—

(A) (i) Is a registered medical practitioner; or

(ii) Is a qualified medical practitioner during his period of provisional registration. Any person so admitted as an associate shall cease to be an associate if he fails to obtain registration within two years of qualification.

(B) Gives an undertaking that he will continue approved postgraduate study if he enters and remains in active general practice, and that he will uphold and promote the aims of the College to the best of his ability.

Criteria for Membership: (A) A person shall be eligible to apply for admission as a member of the College if he—

(i) Is a registered medical practitioner who has been qualified for not less than seven years.

(ii) Is proposed and seconded by two members of the College, these sponsors not being in partnership with each other.

(iii) Has been engaged in general practice either for a minimum period of five years or for a minimum period of three years as an associate of the College.

(B) An applicant for membership must satisfy the Council of the College of the high standard of his work in general practice by—

(i) Evidence submitted by the applicant himself, on an application form, concerning his practice, experience, and academic and administrative achievements.

(ii) Supporting evidence obtained by the Council from the applicant's sponsors, the Board of his Faculty and, if so required, from others whom he or his sponsors have chosen to appoint.

(c) An applicant must also—

(i) Submit himself to an interview with the Censors, if required.

(ii) Give an undertaking that he will continue approved postgraduate study while he remains in active general practice, and that he will uphold and promote the aims of the College to the best of his ability.

Entrance Fees and Annual Subscriptions: As from July 1, 1954, associates shall pay no entrance fee but an annual subscription of one guinea. Any entrance fee which may have been paid by an associate joining after June 30, 1954, shall be treated as being in payment of one year's subscription.

Members shall pay an entrance fee of ten guineas (nine guineas for those who became associates before July 1, 1954) and as from July 1, 1954, an annual subscription of not less than three guineas.

Subscriptions shall be payable in advance.

A *Constitution of Regional Faculties* was amended and agreed, the head of each faculty to be called the Provost.

Officers of New Council

Votes of thanks to Dr. Abercrombie and the first council were acclaimed, and the CHAIRMAN thanked the British Medical Association for its generosity in allowing the College to use its Hall. At a meeting of the second College council, held later, Dr. G. F. Abercrombie was re-elected chairman, Dr. F. M. Rose vice-chairman, Dr. H. L. Glyn Hughes hon. treasurer, and Dr. J. H. Hunt hon. secretary.

Conferences on the postgraduate education of general practitioners and on research in general practice were held the following day.

MEDICAL ASPECTS OF ATOMIC WAR

A CIVIL DEFENCE STUDY AT BRISTOL

Over 150 doctors attended a most successful week-end course at Bristol University, held on November 13 and 14, on the medical aspects of atomic warfare. The course was organized jointly by the South-western Regional Hospital Board and the medical postgraduate department of the university, and the speakers included Home Office experts, distinguished surgeons, and medical administrators.

The course opened with an address by the chairman of the regional board, Sir A. HAVERGAL DOWNES-SHAW, and a short explanation of how the course would be run by Dr. G. C. KELLY, the senior administrative medical officer. Then came a description of modern weapons of war,

including the hydrogen bomb, by a member of the staff of the Scientific Advisers' Branch of the Home Office. With the stage thus set, the meeting proceeded to consider in detail how the various kinds of casualties should be evacuated and treated.

The Civil Defence Plan

Dr. R. L. CHEVERTON (A.S.M.O., South-western Regional Hospital Board) described the Civil Defence plan for Hospital and First-aid Services.

Mobility was the key word in view of the scale of the devastation to be expected after an atomic explosion. In a population of 500,000, there might be 48,000 burn cases to be treated, 40,000 traumatic cases, and 16,000 suffering from the effects of radiation, but the number of injured might be reduced by half if the population made proper use of every kind of cover.

The Mobile First-Aid Unit, consisting of one medical officer (a general practitioner), one trained nurse, and nine auxiliaries, would constitute the first line of medical defence. These units would restrict themselves to the simplest of first-aid measures, all transfusions, shock treatment, and other procedures being carried out at a distance of 10 miles or more from the centre of the incident at cushion hospitals. These hospitals would have 15–20% of their ward space allotted for resuscitation work, and it was not anticipated that cases would remain in them more than seven days, the majority being evacuated after 48 hours.

Base Acute Hospitals, situated 20–50 miles from the catastrophe, would provide general facilities and day-to-day supervision by consultant staff. They would be assisted by the establishment of Base Recovery Hospitals, where cases in need of prolonged treatment, but not needing day-to-day supervision, would be accommodated. The Civil Defence organization also provided for mobile medical, surgical, and resuscitation teams, which would be controlled by a Hospital Group Officer and could be sent to any area or hospital where the need was indicated. The post of Hospital Group Officer was a vital one in the organization, as he would be responsible for the administrative co-ordination of all hospital admissions in the stricken area.

Emergency Surgery

Professor F. A. R. STAMMERS (Birmingham University) spoke of the importance of carrying forward experience gained in past wars and of remembering the part played by environment in the surgical treatment of war injuries. In cultivated areas heavy contamination of all wounds was to be expected. This would remain superficial for the first 6–8 hours, and if possible treatment should be given within this period. As it was vital to keep beds in the forward areas empty, all cases would have to undergo transport to the rear areas, and for this reason no wounds should be stitched, as the journey would certainly result in inflammatory reaction. Adequate splintage would prevent or delay the onset of shock, and delayed primary suture should be performed on about the sixth day with a 90% chance of healing by first intention. Wounds should be cleaned with soap and water or cetrimide and there should be a minimal trimming of damaged skin. Any devitalized tissue and obvious foreign bodies should be removed, the wound should be powdered with penicillin-sulphonamide, and a dry dressing applied.

In his own experience, continued Professor Stammers, three types of wound had proved particularly lethal during the last war. These were the open pneumothorax, the abdominal wound with internal bleeding, and wounds involving major muscle destruction. Full excision was as necessary for a thoracic wound as for any other, and it was vital to keep the thorax "closed" by suture of muscle layers. When large gut was involved, exteriorization was recommended in all cases; and, since post-operative supervision would be inadequate, all abdominal cases should be on gastric suction and intravenous fluids.

Radiation Illness

Sir ERNEST ROCK CARLING, speaking on the pathology and treatment of radiation illness, said that the marrow tissues were most damaged by irradiation. Our knowledge of the normal survival time of circulating white and red cells would lead us to expect loss of resistance to infection in 5–10 days and anaemia after a few weeks. Patients who had been exposed to lethal dosage (600 r in terms of full surface exposure) would complain of increasing headache and dizziness. They would become prostrated, and nausea, vomiting, and diarrhoea would rapidly be followed by fever and death. With smaller dosages there would be an initial improvement, but cell destruction would continue and symptoms would reappear after a delay of 5–10 days. The very young, the aged, and the infirm were more susceptible to the effects of radiation than were the rest of the population.

There was no way of reversing cell destruction once that had occurred, he went on, but drugs which decreased oxygen tension (cysteine, pyridoxine, etc.) might be of prophylactic value. Treatment should consist of rest and nursing, with antibiotics (*not* sulphonamides) as indicated; blood transfusion would be valuable at some stage. A liberal diet should be given before the onset of nausea made this impossible, and the mouth should be kept scrupulously clean in anticipation of the onset of infection. Convalescence would be slow: confident reassurance was invaluable.

Burns

Burns were the subject dealt with by Sir CLAUDE FRANKAU, who emphasized that the measures he suggested were for use in a major catastrophe under conditions when superficial burns of the face and hands would have to be regarded as minor injuries and only deep full-thickness burns could be accepted as hospital cases. For the first group, treatment would be largely a matter of self-help and assistance from friends. Hands should be lightly cleansed, dusted with penicillin-lactose powder, and enclosed in a special transparent, flexible nylon glove which would be available in large quantities. The face might swell after 6–8 hours, so that the patient would be unable to see and would depend on help from friends. Swelling would subside after about 48 hours. Lips and eyelids should be smeared with soft paraffin ointment to prevent sticking, but any lid distortion would indicate the need for expert advice.

Patients with deep burns should be admitted to hospital as soon as possible, and first aid should be restricted to covering the burnt area with clean dry dressings and giving morphine (intravenously) when necessary. Laboratory estimations would not be possible in such conditions, and transfusion needs would have to be assessed by rule-of-thumb methods. Burns involving 15% body surface in an adult or 10% in a child always indicated a need for transfusion, and the burnt area was seldom less when clothes ignited. Plasma was the fluid of choice, but plasma substitutes could be used in an emergency.

Treatment of Shock

Sir HENEAGE OGILVIE considered the treatment of shock. There were many views on the proper definition of this, but he regarded a patient as shocked if injury was followed by a state of collapse characterized by acute circulatory depression. The degree of shock was proportional to the fluid loss, and treatment consisted in replacing the volume lost at the earliest possible moment. For this purpose, plasma substitutes were of limited value, and amounts in excess of 2 pints (1 litre) should never be given. Blood was the fluid of choice, but transfusion of any kind might be impossible in chaotic conditions, and in the field it might be possible to provide only warmth and fluids by mouth. Strong reassurance was of the greatest assistance, and he had found that the patient's own wishes in the matter of warmth and fluids were usually a reliable guide to his bodily needs. A patient who was cold, but did not feel it, should not be

warmed. It was important not to overlook the possibility of internal haemorrhage into damaged tissues.

Panic and War Gases

A number of speakers stressed the importance of the psychological effects of such catastrophes, and this subject was comprehensively dealt with by Dr. W. S. MACLAY. Reliable leaders and the proper use of information services could do much to combat panic, and a belief in his country's cause and a sense of personal patriotism were of value to the man in the street. Fear was the primary cause of mental breakdown in the face of catastrophe and might manifest itself in the form of an acute anxiety state, a depressive state, in hysteria, or in an acute psychotic condition not unlike schizophrenia. Immediate first-aid treatment would consist in giving a good meal and hot drink and sleep under really adequate sedation—for example, sodium amytal, gr. 6–9 (0.4–0.6 g.)—followed by explanation and reassurance.

Surgeon Captain J. G. HOLMES, in the final lecture, discussed biological and chemical warfare. It was probable that aircraft would be the carriers in these fields, and the blister gases were still an effective weapon. The "nerve" gases could be used with effect over large areas, but respirators provided 100% protection. Atropine would be of use in treatment of those who had been affected by such gases.

Major-General W. E. R. DIMOND (Ministry of Health), in his concluding remarks, paid tribute to the very high standard of the addresses given in the course. There had been few professional meetings on this vitally important subject, and he conveyed the thanks and congratulations of those present to Dr. KELLY and Dr. CHEVERTON for their initiative in organizing the conference.

Nova et Vetera

LA VENEXIANA

It was Hippocrates, Rabelais reminds us, who originally suggested that Medicine and the Theatre were of one substance, when he compared the practice of medicine to a conflict and a farce carried on by three characters: the malady, the doctor, and the patient. And certainly there have been many distinguished physicians who have skilfully compounded the arts. Hitherto, however, there has been no dramatic work ascribed to Girolamo Fracastoro (1472–1553), the eminent Veronese polygraph, whose *De contagione* (Venice, 1546) is the first great work of modern pathology, and whose *Syphilis* (Verona, 1530) is at once remarkable for its literary felicity, the acute powers of clinical observation manifested, and the wise and informed prescription of treatment.

Such, too, is the temper of *La venexiana*, which is now thought to be by Fracastoro. This play, of which only one (a sixteenth-century) manuscript is known to exist (in the Biblioteca Marciana at Venice), was first published by its discoverer, Emilio Lovarini, in 1928.

It is set in Venice, and the action takes place almost certainly not earlier than 1510 and not later than 1517. It tells how Iulio, a young Milanese gentleman visiting Venice, and in search of amorous adventures, falls in love with Valeria, a beautiful young married woman whom he sees in church. Meeting her maid by chance he sends his lady an avowal of his love and receives in reply an invitation to come and speak with her that evening. Meanwhile Angela, a widow who is neighbour to Valeria, has become inflamed with desire for Iulio and commands her maid, Nena, to persuade him to come to visit her. She in her turn entrusts the task to Bernardo, an astute and free-speaking porter-cum-smuggler-cum-gondolier, who has little difficulty in coaxing Iulio into accompanying him to Angela's house. Iulio and Angela then become lovers, and spend a passionate night together.

Next day Valeria sends for Iulio and in the course of their ensuing conversation she discovers his faithlessness, for she recognizes a gold chain that he is wearing around his neck as the gift of Angela; and in a fury of hurt pride and jealousy she casts him from the house, swearing revenge, and declaring that she will never so much as look at him again. Iulio is piqued, yet relieved that he has no longer to attempt to satisfy two mistresses.

Valeria, however, quickly regrets her anger and passes a night in tearful repentance, determining in the morning to do all she can to snatch Iulio back from her fortunate rival. He, despite his promises of eternal devotion to Angela, is delighted to accept her surrender, and when Bernardo again invites him to visit his mistress he finds a pretext for refusing. The play ends as Valeria bids her maid close the door behind her as she leaves them together, and warn her husband that she wishes not to be disturbed that night, as she feels a little unwell. . . . And Oria, the thalamic friend, gently closes the door upon the lovers.

The arguments for attributing this play to Fracastoro are almost entirely stylistic, and they have been so convincingly arrayed by Lovarini and by Lentini that it is impossible to escape the conclusion that only the author of *Syphilis* could have written *La venexiana*. There are several indications that the playwright was at least well read in medicine, and I think it is not too fanciful to see him as gently pulling the leg of the Faculty on several occasions. But most important is the fact that throughout the piece one has the sensation of meeting with the same world of experience that illumines not only the *Syphilis* but the entire corpus of Fracastoro's work.

La venexiana is in many respects a startlingly modern play: technically, and in its deep and sympathetic penetration to the mainsprings of human nature and experience, it anticipates the mature Shakespeare. *Not a comedy, nor a fable, but a true history*—that is how the manuscript determines the *Venexiana*. It is a racy, vigorous, and realistic transcript of life, and compelling, splendid, and wholly admirable in its perfect articulation.

FREDERICK MAY.

THE TEXTS

(1) *La venexiana*, ed. Emilio Lovarini, Bologna, Zanichelli, 1928; 2nd edition (revised), Florence, Le Monnier, 1947.
(2) *La venexiana*, translated into Italian (and expurgated) by Lovarini, Turin, Set (now Ilte), 1944. (N.B., the original is in Venetian, Bergomask, and humanistic Italian.)
(3) *La venexiana*, translated into English by Matilde Valenti Pfeiffer, New York, Vanni, 1950 (Lovarini's 1947 text facing the English version).
(4) *La venexiana, or A Comedy of Venice*, translated into English by Frederick May, Leeds, 1954; translation unpublished. Text prepared for production by University of Leeds Italian Society, Spring, 1955.

Reports of Societies

LOCAL MEDICAL SOCIETIES

Manchester Medical Society

Dr. A. R. HUNTER's presidential address to the Section of Anaesthetics on October 21 concerned the incidence of hyperglycaemia, acidosis, and ketosis after anaesthesia. Ketosis, he said, was one of the more important metabolic upsets induced by inhalational anaesthetics, because of its bearing on anaesthesia in the diabetic.

To obtain information on this subject the output of aceto-acetic acid and preformed acetone in the urine during the 24 hours after operation had been estimated in a series of about 150 patients. Ketosis was considerable in those to whom ether or chloroform had been given, but less

marked after cyclopropane, nitrous oxide and oxygen with truly minimal ether, or nitrous oxide supplemented with thiopentone. After spinal analgesia ketosis was usually slight, but a considerable ketone output was occasionally seen in cases in which the analgesic had failed to "take" and supplementary inhalation narcosis had been induced. The same was true of patients undergoing submucous resection of the nasal septum under cocaine and adrenaline.

The severity of the ketosis in adult male patients, who formed the majority of the group, bore no relation to the duration of the operation. The hourly output was found to remain at a high level for some 12 to 16 hours after operation. Thereafter it diminished, but returned to its previous level, presumably because of the development of vomiting in some of the patients, about the twentieth hour of the first day. Ketosis in children was relatively more severe than in adults. In women ketone output was a little higher than the corresponding figure for men.

The correlation between the blood sugar level at the end of the operation and the ketone output during the subsequent 24 hours was very low. The pre-operative administration of 5 to 10 units of insulin had no value in the control of ketosis, but its severity was greatly reduced by 10% glucose given rectally four-hourly during the post-operative period. There was no correlation with the post-operative liver function as measured by Quick's hippuric acid test. These results suggested that the liver glycogen was depleted and the liver fat content increased by the administration of the more "toxic" anaesthetic agents. But neither the findings of this investigation nor the evidence of others supported the idea that ketosis after anaesthesia was due to the production of even a temporary diabetic condition. Dr. Hunter therefore concluded that it was possible to administer the so-called "toxic" anaesthetics to diabetics, provided that suitable amounts of insulin and glucose were given while the patient was unable to take his normal diet.

Speaking on the relationship between benign and malignant hypertension, before the Section of Medicine on November 3, Professor G. W. PICKERING drew attention to the aetiology of the characteristic retinopathy of the latter stage. Recent studies supported the view that the retinal arteriolar necroses, which were the *sine qua non* of the malignant phase, were chiefly the result of a gross rise of intra-arterial pressure, and this led to the suggestion that the malignant phase was essentially a manifestation of a very severe hypertension rather than a disease on its own. If this were so, he continued, it explained the fact that the malignant phase was seen, not only in essential hypertension, but in all known types of hypertension, with the exception of coarctation of the aorta; and also that the malignant phase could be reversed to the benign phase by measures that reduced the hypertension.

Liverpool Medical Institution

The classical peripheral signs of heart failure, said Dr. E. NOBLE CHAMBERLAIN during a symposium on the subject on October 21—venous engorgement in the neck, hepatic enlargement, and swelling of the ankles—often showed no correlation with each other. In children venous engorgement was difficult to recognize, and he found liver enlargement a better sign. With regard to oedema, congestion of the liver produced secondary metabolic upsets which themselves tended to increase fluid retention. The other speakers were Dr. G. A. KILOH, who gave a historical survey of the concepts of heart failure and then went on to discuss low and high output failure, and Dr. E. WYN JONES, who dealt with treatment.

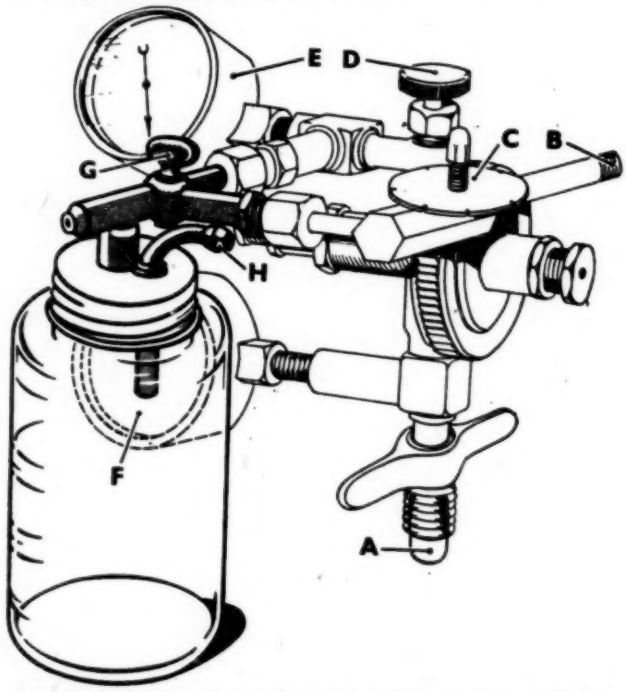
North of England Otolaryngological Society

At a clinical meeting on October 23 at the Cumberland Infirmary, Carlisle, 26 patients were presented, the emphasis being on neoplasms of the nose. Over 50 members and guests took part in the subsequent discussion.

Preparations and Appliances

AN OXYGEN DELIVERY AND SUCTION UNIT

Dr. D. T. CULBERT, consultant anaesthetist, United Manchester Hospitals and Manchester Northern Hospitals Group, writes: Patients with severe bulbo-spinal poliomyelitis should be intubated orally and aspirated and inflated, the tube being left in place for some hours to enable a more accurate assessment of the severity of the paralysis and its effects, as distinct from those of anoxia and hypercapnia, to be made. When skeleton plans were being made to cope with a possible outbreak in the Manchester region, the desirability of having a team prepared to go out and treat an acutely ill patient at home, prior to removal to hospital, was considered. This raised the problem of devising a portable apparatus to deliver oxygen and provide suction, and the illustrated unit was made for this purpose. The unit can, of course, also be used in hospital for oxygen or oxygen–air delivery and for suction.



In the diagram, A is a bull-nosed oxygen-pressure-reducing regulator, F a cylinder pressure gauge, E a flowmeter calibrated up to 12 litres a minute, D the tap regulating oxygen flow from the cylinder, B the point of oxygen or oxygen–air outflow, and H the nipple for attachment of the suction tubing. Control G, in the position shown, allows straight-through oxygen delivery via the Venturi unit, whose control pin valve (C) will, by rotation, give partial air entrainment up to 60% air and 40% oxygen. Stopcock G, when rotated 90°, gives through-suction via H, and when in intermediate positions it provides both oxygen delivery and suction; the greater the percentage oxygen that passes through the Venturi unit the greater is the force of suction. The suction mechanism has proved satisfactory when tried out in the anaesthetics department.

The apparatus has been used in a case of acute polyneuritis with complete bulbo-spinal paralysis, treated in hospital, where the respiratory paralysis supervened suddenly. It functioned in a completely satisfactory manner, and the suction, being slightly less powerful than that of the electrical type, tended to exercise less pull on the pharyngeal tissues.

I wish to thank Dr. R. Ollerenshaw, of the Department of Medical Illustration, Royal Infirmary, Manchester, for the sketch.

This apparatus was made to meet my requirements by the British Oxygen Company.

Correspondence

Haemophilia

SIR,—It has been suggested that patients suffering from haemophilia would find it helpful to carry with them at all times an explanatory card, so as to ensure that any practitioner called upon to treat them in an emergency would be made aware of their clotting defect and would not inadvertently embark on operations or other procedures which might, without preparation, have unfortunate results.

In recent years advances have been made in the diagnosis of haemophilia, and refined tests have been introduced to distinguish this disease from other clotting disorders which, although clinically similar, require different treatment. It is therefore increasingly important that the diagnosis should be conclusively proved before a patient's clotting defect is ascribed to haemophilia. With these objects in mind, the Medical Research Council has joined with the Ministry of Health and the Department of Health for Scotland in preparing a card for issue to haemophilic patients. The names of those to whom a card is issued (see below) will be filed centrally, initially at the offices of the Medical Research Council, and will thus indirectly provide a register which is likely to prove of value not only to the patients but also to research workers. A number of clinics and laboratories have agreed to act as reference centres for applications to ensure that diagnostic standards are uniform, and haematologists in charge of these centres are among those forming the Medical Research Council's Haemophilia Committee.

The following is a preliminary list of reference centres for haemophilic patients. It is hoped to add other centres shortly.

Aberdeen.—Professor H. W. Fullerton, The Department of Medicine, Foresterhill, Aberdeen. *Birmingham.*—Dr. M. J. Meynell, The United Birmingham Hospitals, The General Hospital, Birmingham, 4. *Bristol.*—Department of Medicine, The Royal Infirmary, Bristol. *Cambridge.*—Dr. F. G J. Hayhoe, Haematology Clinic, Department of Medicine, Tennis Court Road, Cambridge. *Cardiff.*—Professor H. Scarborough, Medical Unit, Royal Infirmary, Cardiff. *Dundee.*—Professor R. B. Hunter, Department of Pharmacology and Therapeutics, Medical School, Queen's College, Dundee. *Edinburgh.*—Professor L. S. P. Davidson, Department of Medicine, The University New Buildings, Edinburgh. *Exeter.*—Dr. J. O. P. Edgcumbe, Department of Pathology, Royal Devon and Exeter Hospital, Exeter. *Glasgow.*—Professor L. J. Davis, Department of Medicine, Royal Infirmary, Glasgow. *London.*—Dr. J. V. Dacie, Postgraduate Medical School of London, Ducane Road, London, W.12. *Manchester.*—Dr. J. F. Wilkinson, Department of Haematology, The Royal Infirmary, Manchester, 13. *Newcastle-upon-Tyne.*—Dr. C. C. Ungley, Royal Victoria Infirmary, Queen Victoria Road, Newcastle-upon-Tyne, 1. *Oxford.*—Dr. R. G. Macfarlane, The United Oxford Hospitals, The Radcliffe Infirmary, Oxford. *Sheffield.*—Dr. E. K. Blackburn, The United Sheffield Hospitals, Department of Haematology, The Royal Infirmary, Sheffield, 6.

Any practitioner who has under his care a patient with haemophilia, or one of the closely related diseases such as Christmas disease, and who wishes him to have a card, should apply in writing to the nearest reference centre, enclosing full clinical and haematological findings. If the centre considers the evidence is not quite complete, it may request the practitioner to ask the patient to come for further investigation, preferably as an out-patient. The centre will inform the Medical Research Council of all proved cases of the disease and will issue the haemophilia card to patients through their practitioner. The card contains a statement that the bearer has haemophilia and is under the supervision of a named physician and hospital. It goes on to say: "In case of injury, bleeding, or serious illness this person may have special need of hospital care. The hospital named above or the nearest appropriate clinic should be able to advise on or facilitate admission if informed at once by telephone." The card also contains information about transfusion, blood grouping, and abnormal antibodies. It is believed that, besides safeguarding the haemophilic patient himself and aiding research, the card will be of real value to practitioners called upon to deal with these rare and difficult cases in emergency. Those responsible for the care of any such patients, adult or child, are therefore asked to bring the existence of these cards to the notice of the patient or his parents and to encourage them to permit application to be made for a card.—I am, etc.,

London, S.W.1. H. P. HIMSWORTH, Secretary, Medical Research Council.

Pain on Swallowing

SIR,—With reference to Dr. J. Kohn's letter (*Journal*, November 6, p. 1105) concerning the relief of pain when swallowing in acute pharyngeal conditions, this is a very interesting observation. I would, however, draw his attention to what is known as Wolfenden's position, which gives the maximum relief from discomfort when swallowing in conditions of acute inflammation of the pharynx and particularly larynx. The patient should lie flat face down on the couch with his face over the end and his drink in a glass beneath him. The drink is then sucked up through a tube into the mouth and swallowed. Exactly why this should give such relief it is difficult to say, but anyone who has tried Wolfenden's position when he has acute tonsillitis will testify to the great relief obtained. This manœuvre was, of course, designed for cases of tuberculous laryngitis, now happily much rarer than in Wolfenden's day.—I am, etc.,

Sheffield, 8. E. C. ATKINSON.

Acute Myocardial Infarction

SIR,—Dr. Henry I. Russek (*Journal*, November 6, p. 1104) again reminds us that the "good risk" case rarely develops thrombo-embolism, but I believe that he overstates the risk of anticoagulant treatment, properly controlled, in this very class of patient. The liability to accidental haemorrhage goes hand in hand with the likelihood of occlusive vascular complications, and the "good risk" case is an even better risk in respect of coumarin—induced bleeding. For example, in my series (*Journal*, July 4, 1953, p. 4) of 406 patients treated with anticoagulants there was not a single instance of serious haemorrhage among the "good risk" cases, and I have not seen one since. Improved drugs and a powerful antidote have appeared since this series was started.

While the risk of haemorrhage is negligible in this group of cases, that of over-optimistic prognosis is not; it occurred to the extent of 1 in 20 of Russek's series. On this reasoning it is unnecessary to attempt such differentiation on prognostic grounds when the contraindications to anticoagulants are faithfully observed and control is adequate. The margins of probability are small, however, and there are important economic and personal considerations which influence the choice of treatment. Thus, in my view, it is generally better to concentrate the available facilities for anticoagulant treatment on the more serious type of case and to leave the "good risk" patient at home.—I am, etc.,

London, N.19. H. E. S. PEARSON.

Radial Carpal Syndrome

SIR,—Explanation of the patient's complaint of abnormal sensations in the hand is a frequent diagnostic problem. In trying to differentiate between the causes arising in the hand the median carpal tunnel syndrome is probably foremost in mind, and secondly the pressure neuritis of the ulnar at the pisiform. I have not seen mentioned what I suggest might be called "radial carpal syndrome." The paraesthesiae occur in the distribution of the terminal branch of the radial nerve below the wrist; rubbing in the anatomical snuffbox reproduces the sensation in the skin of the radial side of the thumb and the adjoining part of the thenar eminence (the abnormality is of course only sensory). The especial importance of considering this radial irritation is the avoidance of a disappointing median operation with its unsightly scar.—I am, etc.,

Barnes, S.W.13. GEOFFREY HOVENDEN.

Toxaemia of Pregnancy

SIR,—Dr. Katharina Dalton's observations on this subject (*Journal*, November 6, p. 1071) open some fascinating new vistas for understanding toxaemia and some of the convulsive states. Study will now be directed to treating toxaemia along these new lines. Perhaps it is opportune, therefore, to discuss whether an assumption that premenstrual and therefore pre-eclamptic women merely lack progesterone may not prove to be an over-simplification. Clinical evidence is available which suggests that at any rate premenstrual tension may depend more upon the presence of some *special adverse ratio of the steroid hormones to one another* than upon any simple deficiency of progesterone. Unfortunately, a "ratio" of such a nature is a most elusive entity to assess or to correct: and it may be exactly for this reason that there is so much contradictory teaching on these matters. By means of other steroids, too, it is sometimes possible to relieve not only premenstrual tension but other somewhat allied disturbances such as pregnancy sickness, menopausal tension, and even puerperal and involutional melancholia as well. The fact that such syndromes can on occasion be relieved in diametrically opposite ways suggests that the steroid balance is by no means always deficient on the side of progesterone. Indeed, without a postulate of some shifting balance it is hard to see why one case of premenstrual tension can be relieved by such small doses of progestogens, whereas another, apparently equal in severity, may require the very heavy dosage which Dr. Dalton has sometimes needed to employ.

It is easy to show that methyl testosterone, 5–10 mg. daily, may sometimes relieve premenstrual tension dramatically, and oestrogen taken in the first half of the cycle, or sometimes even during the premenstrual days, will often do likewise. Thus the wife of a colleague resorts regularly to oestrogens during her highly uncomfortable premenstrual days as well as in her severe pregnancy sickness. Let anyone who doubts these responses treat his next six cases of premenstrual tension with oestrogen during the first 18 days of the cycle. Natural oestrone *B.P.C.* should be chosen, since the synthetic products, being toxic to such a high proportion of women, readily confuse the issue. The dose need not be more than 1.5 mg. daily for women under 45, or 1 mg. daily for those over that age. Some of the cases will almost certainly be relieved. Clinical reports of these responses have been published in many different quarters, and they may be of value in the understanding of pregnancy toxaemia as well. I have discussed in some detail the postulate of an adverse steroid ratio and its usefulness in managing various malaises of women,[1] and since then have been offered confirmatory evidence for this view by various colleagues.

There are difficulties in estimating clinical data of this sort. For example, it is accepted that hormonal substances can produce contradictory results in different doses, on the principle that "a little may stimulate and a lot depress." Moreover, the use of any one of the sex hormones may introduce new reactions by altering the trophic stimulation of the other steroids. So long as the laboratory measurement of steroid balance remains so unpractical our methods of dosage and rationale have to be based largely upon the patients' subjective responses. Dr. Dalton's emphasis on the changes in weight and blood pressure should therefore prove especially helpful to future study.—I am, etc.,

London, N.W.1. JOAN MALLESON.

REFERENCE

1 *Lancet*, 1953, 2, 158.

SIR,—Dr. Katharina Dalton (*Journal*, November 6, p. 1071) has made an important contribution to the problem of toxaemia of pregnancy inasmuch as she has demonstrated the effectiveness of progesterone in its treatment. In a joint contribution[1] she had previously shown a like beneficial effect in treating premenstrual tension. The revealed inadequacy of progesterone was held to indicate that it had failed to meet a demand, which, unsatisfied, gave rise to either premenstrual tension or to pre-eclampsia. An explanation of these findings and their correlation with the thesis that the utero-renal reflex underlies the aetiology is made available when examining Schultze's[2] researches. By measuring the intrauterine pressure changes effected by the sudden introduction of fluid he determined the distensibility of the human uterus at various periods of the menstrual cycle, and the results helped him to plot a "tension curve" which was characteristic of the uterus *of any given woman*, although it varied with the parity of the individual and the phase of the menstrual cycle. The stretching capacity appeared to be greatest during menstruation, intermediate in the luteal phase, and least of all in the early or mid-interval. Oestrogen therefore heightened myometrial tension. Corner and Csapo[3] have also demonstrated that the isometric tension of the uterus is much increased in the oestrogen phase and have correlated this fact with an increased adenosine production as well. Circulating adenosine[4] is responsible for reduced glomerular filtration. This substance has been demonstrated in the blood of the toxaemic patient and has been held to be an index of uterine ischaemia,[5] the result of heightened myometrial tension, which in its turn provides the stimulus for the production of the utero-renal reflex[6] and provokes renal ischaemia, the basis of the pre-eclamptic symptomatology.[7] Wade and Jones,[10] however, have shown that progesterone inhibits human endometrial adenosine, and this may well provide the explanation of Dr. Dalton's therapeutic success.

Primiparity has been shown by Reynolds[8] to be characterized by a heightened uterine tension as well. Sighting shots[9] with oestrogen in the rabbit revealed that renal ischaemia could result from its exhibition, though progesterone was without effect. In view of this evidence, Dr. Dalton, in providing a useful method of therapeusis, has indirectly served to correlate myometrial tension with the symptomatology both of premenstrual tension and pre-eclampsia.—I am, etc.,

London, W.1. JOHN SOPHIAN.

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6 Sophian, J. (1953). *Toxaemias of Pregnancy*, p. 45. London.
7 —— (1954). *Reports of International Congress of Obstetrics, Geneva*, p. 822.
8 *Contr. Embryol. Carneg. Instn*, 1951, 34, 75.
9 Franklin, K. J. (1954). *Reports of International Congress of Obstetrics, Geneva*, p. 819.
10 *Obstet. Gynec.*, 1954, 3, 608.

SIR,—With reference to the interesting essay on toxaemia of pregnancy by Dr. Katharina Dalton (*Journal*, November 6, p. 1071), I should like to suggest that the cause of their unfortunate malady would appear to be more complicated than a simple deficiency of progesterone, since a hydatidiform mole is associated with excessive increase of lutein tissue and anterior pituitary-like substance in the urine, and yet may be accompanied by severe toxaemia of pregnancy.—I am, etc.,

London, S.E.1. R. G. ORR.

Death Due to Chloramphenicol

SIR,—Dr. D. Gairdner reports another case of chloramphenicol causing death (*Journal*, November 6, p. 1107). A further point arose with a recent case of ours.

A boy aged 11 years was admitted to hospital on September 18. There was a history of antral infection for several years and a chest infection for some months. On admission his white cell count was 6,720 per c.mm.; polymorphs 60%, lymphocytes 35%, monocytes 5%. Friedländer's bacilli were found in the sputum. He was treated with a five-day course of chloramphenicol, 1 g. a day. Routine white cell count on October 12 was: total 3,520 per c.mm.; polymorphs 17%, lymphocytes 79%, monocytes 4%. Treatment of the leucopenia was given next day: one compound penicillin injection 1,200,000 units "pentnucleotide" 10 ml. and cortisone 50 mg. He developed no symptoms. On October 14 the total white cell count was 5,440 per c.mm., with polymorphs

57% rising next day to total 8,320 per c.mm., polymorphs 75%. His chest infection cleared, and following antral irrigation he was discharged on October 29, a final white cell count being normal.

This child's leucopenia was temporary and disappeared rapidly. A second dose of chloramphenicol, no matter how small, would no doubt precipitate a fatal agranulocytosis. In general practice this leucopenia might have been missed.—I am, etc.,

Dublin. ELINOR D. U. POWELL.

M'Naghten Rules

SIR,—Perhaps I may be permitted, a little late in the day, to reply to my many critics in your correspondence columns. What most of them found so objectionable were things that they imagined I was saying, but which in fact I did not say (*Journal*, September 25, p. 713). I made no attack, for instance, on our concepts of right and wrong; I did not imply that stealing by finding was excusable; I did not assert that actions were not influenced by moral considerations. If they doubt this, perhaps the critics would read the article again. None of those issues has any direct connexion with the question whether "responsibility" can be given an objective meaning, which was the question under debate.

It is clear that a principal subject of offence lay in the sentence: "The 'free will,' on which both law and religion are based, proves a heuristically sterile idea." Your correspondents seem to have imagined that I was asserting that "free will" does not exist, when all that was said is that it cannot be used scientifically—for example, in an attempt at analysis of the causes of behaviour. If they doubt the truth of this very limited statement, perhaps your correspondents, or one of them, would provide the plan of an experiment which would show the presence or absence of free will in the actions of experimental subjects. My position is that no such experiment can be imagined.

Free will is a much more difficult concept than most of your correspondents realize. The determinist would not maintain, as Dr. Reginald Fisher (*Journal*, October 16, p. 929) naively supposes, that he wrote that letter because he was "made that way" and he had to, but much more simply because he wished to and had reasons for his wish. We all of us assume that, if people are left to act freely, they will do the things they want to do; and in taking that attitude we are in practice siding with the determinists. Whether "free will" corresponds or does not correspond to a metaphysical, if not objective, reality is a question we should do well to leave to philosophers.

I should like, finally, to comment on a matter of spelling. Although the variant "M'Naghten" has long been used by the *Journal*, and was adopted in its Report by the Gowers Commission, that Commission in the course of its inquiries unearthed evidence that the man himself wrote his name "McNaughton," which form therefore would seem to have the best authority.—I am, etc.,

London, S.E.5. ELIOT SLATER.

SIR,—Dr. Eliot Slater's article (*Journal*, September 25, p. 713) on the M'Naghten Rules was in many ways not only stimulating but constructive. However, like the majority of my psychiatric colleagues to-day, he regards all behaviour as relative. This is in fact a dangerous fallacy. But it ceases to be so if the majority of people regard the existence of God as a delusion, even if a necessary one.[1] In fact, if there is no power higher than man, to deny the existence of absolute values in the world of behaviour is perfectly logical; but "the fool has said in his heart, there is no God" (Psalm 14, verse 1).

The increasing rise of anxieties, wars, and distress of all kinds, in spite of the miracles of scientific progress, should be sufficient warning that we ignore God at our peril. Professor Outler[2] has shown most eloquently how immensely valuable is psychiatric knowledge if only it is used, as all knowledge, of whatever kind, should be, without violating the absolute revealed truth found in Holy Scripture, which is the inspired word of God; always remembering that the cornerstone is Christ, the Saviour from sin, and that the Old Testament must be interpreted in the light of the New.

Dr. Slater is right to press for a revision of the N'Naghten rules. As a psychiatrist I agree that it is obvious that all behaviour is determined by events that have gone before. Our job then should be to decide to the best of our ability whether the psychological events in the patient's life were such as to overcome his ability to exercise control over his impulses. Wrongdoing itself is never right. The act of stealing or murder is still sin whoever did it, and under whatever circumstances, not, as Dr. Slater seems to think, a matter of changing custom. In the eyes of God the pocketing of the half-crown is an infringement of the moral law exactly as is murder.

As an analytically orientated psychiatrist I can assure Dr. Slater that I am in the forefront of any movement to reduce harsh emotional prejudice towards the mentally ill who, because of their illness, infringe the civil or criminal law (which is not always identical with the moral law). However, the tendency of our branch of medicine to destroy belief in God and His divinely revealed will for our salvation and true happiness through Christ is a dangerous deceit of the Devil which will in the end more than nullify the great benefits that all types of psychiatric treatment are bringing to mankind.—I am, etc.,

Selkirk, Manitoba. H. B. KIDD.

REFERENCES

[1] Masserman, J. H. (1953). *Amer. J. Psychiat.*, **110**, 324.
[2] *Psychotherapy and the Christian Message*, 1954. Harper, New York.

SIR,—Why should Dr. Eliot Slater's statements about responsibility in his article (*Journal*, September 25, p. 713) on the M'Naghten Rules interest us at all and provoke us to correspondence? Because men know, and have known through the ages, that people are not always wholly responsible for their actions. From this appreciation arises our concept of tragedy, and, speaking sociologically, the necessity to determine where responsibility ends and insanity begins.

It seems to me that this sociological problem with its medical implications is exactly what Dr. Slater goes some way to clarify in his article. As for his statements about free will and determinism, I should also like to quote him: "No theory of mental medicine could develop without the *working hypothesis* [my italics] of determinism. When a man acts in a given way at a certain time under a particular set of circumstances we must assume, if we are going to understand his conduct at all, that it was determined by such things as his own make-up, his physical and mental state at the time, and the circumstances and his appreciation of them." This does not sound very different from the method used by every physician in assessing disease. Would we not approach a person presenting the symptoms of congestive heart failure in exactly this way, except that the major emphasis would be on the physical aspects? If we assume that mental activity arises from the brain, surely there is every justification for applying this same scientific method of investigation to mental symptomatology.

The correspondents up to November 6, writing about Dr. Slater's article, seem as determined to ignore the unconscious as they find him determined to discard free will. In our understanding of behaviour I believe we have advanced since Dr. Johnson's time, possessing, as we do now, this useful concept of the unconscious mind. The fault may well lie "not in our stars but in ourselves"; unfortunately, however, in many instances, in our unconscious selves. Concerning what the individual is not aware of (and by definition he does not know what is in the unconscious part of his mind) he is surely in no position to exercise free will. Psychiatrists subscribe to "free will" to the extent that they attempt to bring the disturbing elements of the unconscious under the patient's conscious control. They should have to abandon any idea of treatment if they believed their patients did not have, and never could have, any degree of choice.

I doubt if any of us would hold a person "responsible" for the content of his dreams, which is now generally regarded as being beyond conscious control. But when the result of unconscious mental activity becomes not dreams but criminality, we rush from our outposts of learning back into the emotional jungle. We might do worse than pay some attention to Dr. Slater's constructive suggestions about "fitting the punishment to the criminal" as well as to the crime.—I am, etc.,

London, S.W.3. JEANNE JOHNSON SMITH.

Appendicectomy in Chronic Appendicitis

SIR,—Dr. H. D. Forbes Fraser (*Journal*, October 30, p. 1049) was evidently so emotionally disturbed by the implications of the first sentence of my letter (*Journal*, October 9, p. 869) criticizing the paper by Mr. Iain McLennan and Mr. J. Kennedy Watt (*Journal*, September 25, p. 736) that he was unable to read clearly the words that followed. I merely intended to point out that the authors did not present a convincing argument that chronic appendicitis is a clinical entity. Only 65% of their patients were *completely* cured of their abdominal pain by the operation, and an unknown number of these may have sought refuge in other symptoms such as headache or backache now that the appendix could no longer be incriminated. Nevertheless suggestion alone will be bound to cure many; Dr. Forbes Fraser is quite wrong when he infers that deeper psychotherapy is always required to relieve functional symptoms. No doubt he is doing this by simple reassurance every working day. Whether it is justifiable to use an operation for this purpose has not been decided by the paper, because the authors did not include a control series in which reassurance, backed up if necessary by special investigations, was the main treatment.

In children functional abdominal pain, masquerading under many labels such as spastic colon, constipation, abdominal migraine, mesenteric adenitis, etc., is very common, especially near scholarship examinations and other times of stress. The whims of the surgeon and/or the fears of the parents (as with circumcision) often carry more weight in deciding the issue of appendicectomy than the actual condition of the child patient.—I am, etc.,

Stock, Essex. IAN G. WICKES.

A Penalty of Partial Gastrectomy

SIR,—I was much interested by the letter of Mr. James A. Ross describing one of the less well recognized penalties of partial gastrectomy (*Journal*, October 30, p. 1049), and, although readily admitting its reality, I cannot share his surprise at the fact "that a doctor, knowing the technical details, and conversant with modern literature, should have concurred with the adverse opinions of the laymen" who informed the partially gastrectomized seeker of employment that "after a stomach operation he was not considered fit to undertake the duties of a commercial traveller." I was a final year medical student only a little more than two years ago, in the very teaching hospital from which your correspondent writes, and I still frequently refer to a particular set of lecture notes which I took down from one of the most eminent lecturers in medicine at that time. At one point these stress, in very definite terms, that the finals candidate, when posed the question of the pros and cons of medical and surgical treatment of the duodenal ulcer, should always remember that a man can never regain his old standard of normal health after partial gastrectomy; and that many workers, particularly manual, will never be fit to return to the same job again. I grant that the lecturer here was a physician, and not a surgeon, but he was a man whose word in the sanctity of the lecture theatre was taken as law. It can be guaranteed that all students graduating that year would leave their alma mater carrying away the indisputable dogma that the partially gastrectomized man will, very often, never again be fit enough to return to his old job.

I have been fortunate in spending most of my time since qualification working in surgical units turning out and following up veritable streams of partially gastrectomized men, and I soon had no alternative but to conclude from the ample evidence before my eyes that on one point, at least, my teacher had misled me: the great majority of men after partial gastrectomy are actually fitter for their particular job than before. Unfortunately, most graduates cannot have the opportunity of seeing such series of cases for themselves, and so they must go on practising in accordance with their teaching. The particular physician I quoted from is, of course, far from being an isolated example, and there is, without doubt, still an appreciably large school of thought which is extremely sceptical concerning the degree of efficacy of the operation in question. Although, as I see it, there has not been any outstandingly significant, or widespread, change in the technique of partial gastrectomy in this country over the last few years, I do think that, in those few years, the operation has definitely been progressing, more rapidly than previously, in its gaining of a more widespread appreciation for its genuine merits. If my humble opinion can be of any cheer to Mr. Ross, I would conclude by venturing a prediction that the appreciation of the true worth of the operation will thus soon have spread to the farthest corner of the sceptics in the profession, and then surely even the lay employer must soon see the light.—I am, etc.,

York. D. G. CHAMBERS.

Treatment of the Common Cold

SIR,—"Starve a fever, feed a cold" is an old saying in which may be the answer to the treatment of the common cold. Although it does not give a choice of food, a clue is to be found in the pre-war claim much advertised by the orange growers. More recently it has been suggested that heavy doses of ascorbic acid were effective. However, this did not seem to be the complete answer. By chance I noticed that a combination of the vitamin-B complex taken in combination with heavy doses of ascorbic acid seemed to abort the common cold in 24–48 hours; also a smaller dose can be taken prophylactically. This observation seems to be so consistent that I felt that it was worth while making it more widely known. Dosage: ascorbic acid, 200 mg. four-hourly, and vitamin B compound tablets three times a day.

In order to substantiate this claim I gave a small series of cases a course of the two vitamins and a series of controls were given dummy tablets. Day-to-day records were made and nose and throat swabs were taken as a routine at the first inspection. In all cases no pathogenic organisms were demonstrated. Of the 12 recorded cases given genuine tablets, 11 were fit on the third day, one case went home and was not seen for two weeks. Of the 10 cases given dummy tablets, five were considerably worse on the sixth day, one was fit on the fourth day, and one was fit on the second day. The other three did not attend again. Other cases have been treated but not recorded, and the impression is favourable when compared with other forms of treatment.

Although I can only offer my own observations as proof, the results have been so dramatic that I feel that others should be given a chance to try it.

I wish to record thanks to Messrs. Lawrence and Scott, Norwich, for allowing me use of their sick-room and the men for attending; also to Roche Products for supplying the tablets.—I am, etc.,

Norwich. A. S. WOOLSTONE.

Fallacy of the Furred Tongue

SIR,—Dr. B. Gans's attempt to expose the "fallacy of the furred tongue" (*Journal*, November 13, p. 1146) is unconvincing and misleading. He does not distinguish adequately between types and degrees of furring, nor indeed does he define what he means by a furred tongue. He does not give us the numbers of "sick" and "normal" children among the 750 he examined, yet no less than 468 of their tongues, or 62.4%, were furred. Is this the proportion of furred tongues in the population as a whole? Where, in fact, is his normal control series? Further, Dr. Gans is guilty of a misuse of statistics. He classifies his diagnoses into 11 headings as if these were mutually exclusive. Are we to believe that none of the children with emotional upsets, skeletal abnormalities, and skin troubles were suffering from upper respiratory infection or digestive troubles, two

categories in which he admits the possibility of a positive correlation? Yet even under these two headings he makes no attempt to break down the diagnoses to show where the correlation may lie, even though the headings are so broad as to be meaningless—for example, "constipation, herniae, 'tongue-tie,' . . . healthy infants." To the too-wide mesh of statistical tables I prefer the wisdom of the ages, and I hope that doctors will continue to examine their patients' tongues.—I am, etc.,

London, W.C.2. H. I. WINNER.

Industrial Dermatitis

SIR,—The correspondence following Dr. F. Ray Bettley's article entitled "Some Current Problems in Industrial Dermatitis" (*Journal*, October 16, p. 905) and the "Any Questions?" item "Oil at Work" in the same issue (p. 938), is of considerable interest, particularly as the Barrier Substances Subcommittee of the B.P. Codex Revision Committee has now issued suggested formulae for standardization of barrier creams.[1] One would agree with the statement that "oil itself is seldom a sensitizing agent," but I have yet to examine a soluble oil which has not been altered in some way, usually with the addition of phenolic compounds, potash soaps, etc., and similarly the insoluble oil may vary greatly in composition and may contain sulphur and even chlorinated hydrocarbons.

After having tested barrier creams for many years against both soluble and insoluble oils on thousands of workers,[2,3] I have found that, properly used, barrier creams are effective, and experimentally it has been shown that adequate protection is possible, as Puccinelli and Vigliani[4] (the combination of dermatologist and professor of industrial medicine) state: "Taking advantage of the intense fluorescence of mineral oils in Wood's light we observed that, after soiling with oil and successively cleansing and washing, the oil residue on the skin protected by a barrier cream widely used in Italy ("kerodex") was minimal as compared with the oil residue on unprotected skin; the experiment shows that the barrier cream employed possesses good isolating properties which prevent the oil from penetrating and remaining in the follicles. The clinical results of the use of the same barrier cream in industry has demonstrated that where the cream has been applied systematically, strictly observing the instructions for its use, it is effective in preventing oil dermatitis. Where the skin is subject to intense friction, the cream must be applied every two hours of work." This does not agree with the earlier experiments of Cruickshank.[5]

Further evidence that barrier creams are effective enough to warrant official support is the fact that the B.P. Codex Committee, consisting of pharmaceutical, dermatological, and industrial medical authorities, have now published a range of formulae for barrier creams as follows: A, Dust barrier. B. Water barrier. C. Oil and solvent barrier. D. Skin conditioning cream. The provisional formula for the oil barrier is: kaolin (sterilized), 20; bentonite, 3; hard soap (powdered), 12; glycerin, 6; stearic acid, 2; sodium chloride, 1; chlorocresol, 0.2; phenol, 0.5; distilled water to 100. It is difficult to appreciate how this is going to protect against soluble oil which may contain as much as 95% water, as the cream is itself water soluble.

It is to be hoped that the committee which sponsors these formulae will undertake to issue specific instructions as to correct use. The committee must also take upon itself the responsibility of supplying information as to the range of substances against which these creams will be effective, and such information must be supported by strong evidence before practical experiments in factories can be carried out, as the common-law risk is still the liability of the employer, and nothing could be worse publicity than the results of poor protection. With reference to Dr. E. Collier's statement (*Journal*, October 30, p. 1047) that the barrier cream "must have a specific neutralizing action on the particular skin irritant involved," I feel that few dermatologists will agree with this. There should be no chemical reaction permitted to take place on the skin. One of the cardinal principles of barrier cream protection is to prevent this occurring.

In a series of some 280 cases seen at the Royal Northern Hospital and at medical boards in the past 12 years about 66% came from factories with less than 200 workers. Industrial dermatitis is not common in large factories with good supervision unless some new unsuspected hazard is introduced, an example of which is the difficulty now being met with in the use of the amines as catalysts in the newer thermo-setting plastics. Patch-testing is of very doubtful value, as a skin already sensitized can give the most divergent results. It is usually easy to show that where there has been a considerable area of dermatitis, patch-testing elsewhere on the same skin with relatively innocuous substances can give fresh erythematous areas. I have known this occur when testing with a barrier cream which contained a minute amount of cetrimide. The dissatisfaction expressed by Dr. M. E. M. Herford (p. 1047) is real. If the cases of dermatitis of alleged industrial origin were seen by those with an adequate knowledge of the industry as well as the dermatologist, surely a diagnosis acceptable to all interested parties would be obtained.—I am, etc.,

London, N.5. L. B. BOURNE.

REFERENCES

1 *Chem. and Drugg.*, 1954, 162, 412.
2 *British Medical Journal*, 1944, 2, 57.
3 Ibid., 1944, 2, 290.
4 *Atti del Convegno Internazionale di Medicina del Lavoro*, Milan, 1950, p. 121.
5 *Brit. J. industr. Med.*, 1948, 5, 204.

Changing Aetiology of Heart Disease

SIR,—Professor W. Melville Arnott (*Journal*, October 16, p. 887) thinks it unlikely that mental stress plays any part in the causation of coronary artery disease. He reasons thus: Disproportionately many of the victims are of the professional class. Stress, on the other hand, is not selective. The basic emotions, the capacities to "'feel' emotionally . . . to love, to hate, to fear, to hope," are felt alike by all mankind. Plainly so much is true—for these particular emotions. Equally it could be said that people's native intelligence appears not to vary widely. Certainly gallantry and fortitude are not confined to any one social class.

But all this is irrelevant. Professor Melville Arnott goes further. In his view, "to think deeply" and "to aspire" are habits no less universal. Now to believe this is to deny all human experience. In this country to-day the extreme prosperity of the picture papers, "Workers' Playtime," and the football pools illuminates the popular intellectual taste with incontestable clarity. The fact is that the sterling virtues of the majority of our citizens find expression in a few simple fundamentally decent instincts. They remain uncomplicated by the slightest inclination towards abstract thought. It would be much nearer the truth to say that this majority prefer to keep their thinking at a comfortable minimum. As for personal ambition, they regard it with active hostility. Perhaps one-tenth of the population is subject to the special stress that goes with competition and effort directed to individual as against group advancement. In numbers this class has, nevertheless, been greatly enlarged by secondary education, accompanied by a simultaneous loosening of traditional religious and social constraints. These forces have been at work for the last 50 years or so. This is also the period during which coronary disease has made its dramatic increase. In doing so it has shown a remarkable predilection for the newly expanded professional class. Here, then, is an interesting parallel. Maybe it even suggests an hypothesis—admittedly no more than the most modest and tenuous wraith of a thing.

All the same there seems little need for it to fear comparison with the theory, more favoured apparently by Professor Melville Arnott, that seeks to identify a causative factor in degree of physical activity. The investigation recently carried out by Morris *et al.*[1] purported to show that fatal coronary disease occurred significantly more frequently, and angina less frequently, among "inactive workers" as compared with an otherwise similar "active" group. Yet the angina of degenerative heart disease commonly begins suddenly. This is taken as good evidence that the symptom has then resulted from a small acute infarction. Morris's findings, then, point to the conclusion that

activity tends to prevent big infarctions, which might be reasonable enough, while at the same time provoking small ones—a paradox so bizarre that it must surely throw doubt upon the value of the evidence.

Coronary artery disease, its pathology, and the factors controlling its clinical manifestation are of course still a mystery. Some influences seem to have bearing upon it: in particular age, sex, heredity, occupation, and hypertension. And some associated problems are obvious—for instance, those of blood-clotting, hormonal influence, and the selective siting of atheroma. Some day no doubt the determinant aetiological clue will be identified—possibly in the form of a dietary constituent. But perhaps no one need be surprised if its origin should prove to be psychogenic.—I am, etc.,

Blackpool. I. McD. G. STEWART.

REFERENCE

[1] *Lancet*, 1953, 2, 1053.

International Anatomical Nomenclature

SIR,—May I remind Dr. H. Williamson (*Journal*, October 30, p. 1051) that in July, 1952, following the first meeting of the International Anatomical Nomenclature Committee, I sent you a summary of the programme which the committee had undertaken (*Journal*, July 5, 1952, p. 41), and I invited clinicians, physiologists, pathologists, and others interested to communicate with me on the matter, promising that any suggestions made would receive serious consideration from the particular subcommittee concerned? The number of letters I have received on the subject, excluding those from fellow anatomists all over the world, indicates that my letter aroused little interest amongst clinicians in this country, but I would emphasize that the committee laid stress on the fact that all anatomists in all countries should regard themselves as free to translate any new (or old) Latin terms into the equivalent in their own vernacular for teaching purposes. We asked from clinicians and from medical scientists generally that they should, if the nomenclature is approved by the Paris Congress, in future use the terms *in their Latin form*, especially in the *titles of communications, monographs*, etc. Throughout our meetings we have constantly borne in mind that, if it is approved, the list of terms must concern medical students, and our aim has been to simplify where simplification has proved practicable. Our proposals are conservative, and we hope that they will not lead in any country to an increase in the difficulties with which the modern medical student is faced.

Further, we propose to ask the Paris Congress to set up a small standing international nomenclature committee to consider and decide on any subsequent proposals for changes, subject to the approval of the next International Congress of Anatomists. Let me say, too, that, although it is now too late to modify the report which will be submitted to the Anatomical Congress in Paris next July, any helpful suggestions which may be received hereafter will be retained and duly submitted to the standing committee, referred to above, when it is appointed. Is there any other way in which we can help?—I am, etc.,

London, S.E.1. T. B. JOHNSTON,
Honorary Secretary,
International Anatomical Nomenclature Committee.

Flourpaper Tuberculin Jelly Test

SIR,—In commenting on the unreliability of the flourpaper tuberculin jelly test, Dr. W. H. Tattersall (*Journal*, November 6, p. 1105) states that there is an urgent need to evaluate the accuracy of the Heaf multiple puncture method of tuberculin testing.[1] We have used this method regularly for over three years for the preliminary screening of medical students and nurses, while retaining the Mantoux test (100 I.T.U. old tuberculin, and more recently 10 I.T.U., P.P.D. tuberculin) as a final check on non-reactors immediately prior to B.C.G. vaccination six weeks later. We have, therefore, a basis for assessing the accuracy of the multiple puncture technique.

We have used the method in approximately 1,650 cases, of which 910 were carried out with a view to possible B.C.G. vaccination; of these, 683 were definite positives, 16 doubtful positives, and 211 negatives. The doubtfuls were retested by the Mantoux method and all 16 gave definite positive reactions. It appears that delayed reactions are not uncommon with the multiple puncture method, and some of our "doubtful positives" were in the early days when we read them at 48 hours. We now prefer to wait at least three days, and conclude that a multiple puncture test should not be read at less than 72 hours, and that any degree of induration at this time can be regarded as positive. The two methods are compared in the following table:

	Preliminary Screening Test	Repeat Test on Non-reactors after 5–6 Weeks
1949–51 ..	Mantoux to 100 I.T.U.: Negative 177	Mantoux 100 I.T.U.: Negative 174. Positive 3
1951–4 ..	Heaf: Negative 211 Doubtful: positive 16	Mantoux: Negative 208. Positive 3 Positive 16

In each series three cases are recorded as having become positive after a six-week interval. One or two of these were probably coincident natural conversions, but, in so far as the others were due to errors in technique or interpretation, the discrepancy was no greater with the multiple puncture method, and with longer experience we now find it presents less difficulty in interpretation than does the Mantoux test. It is concluded that the method is accurate as well as economical and convenient. It is much preferred by the patients, while the single return visit and the latitude permissible in the time of reading the reaction (three to seven days) are strong points in its favour.—I am, etc.,

Sheffield, 10. P. W. W. GIFFORD.

REFERENCE

[1] *Lancet*, 1951, 2, 151.

SIR,—In his letter on tuberculin testing (*Journal*, November 6, p. 1105) Dr. W. H. Tattersall has stated that it is a matter of some urgency to evaluate the Heaf multiple puncture test as speedily as possible because of the growing lack of confidence in the modified jelly test. I therefore desire to present the results obtained with the Heaf test in a clinic of this department, where it has been used since February of this year for screening candidates for B.C.G. vaccination. The children who were tested were aged from a few months to 16 years, their total number being 1,345. The reactors numbered 360, and the remaining 985 were immediately Mantoux tested (100 T.U. of old tuberculin). The following were the results:

Result of Heaf Test	No. of Persons	Result of Mantoux	No. of Persons	Percentage
Negative ..	938	Negative ..	933	99·5
		Positive ..	5	0·5
		Total ..	938	100
Doubtful ..	47	Negative ..	39	83
		Positive ..	7	14·9
		Doubtful ..	1	2·1
		Total ..	47	100
Total ..	985		985	

It is thus seen that in this series of children there was almost complete agreement between the negative Heaf and the negative Mantoux, and it should be remembered that with a dose of 100 units of old tuberculin some of the resulting Mantoux reactions are likely to be false positives. Two of the children who were recorded as Heaf-negative and Mantoux-positive were the first two children to have the Heaf test, and in the light of subsequent experience the reactions they displayed would not now be classed as negative.

The number of doubtful reactions (4.8%) was unduly high. It is explained by inexperience of the instrument,

for we have now learnt that when doubtful reactions are seen it is time to fit a fresh battery of needles. Blunt needles injure the skin in such a way as to cause a reaction to the trauma which can be mistaken for a reaction to tuberculin. No unduly severe reactions were seen in the children, but several hospital nurses were annoyed by their reactions, a small area of necrosis of the skin occurring in the centre of the confluent papule. Reactions may remain visible and palpable for several months. A control Mantoux test of the children who reacted to the Heaf test was not made.

I am indebted to my colleague, Dr. R. Linton, for carrying out most of the above tuberculin tests.—I am, etc.,

Belfast. H. G. CALWELL.

Cancer Resistance

SIR,—In a letter to the *Journal* (May 8, p. 1095) Dr. A. Wiseman concludes that there must be some resistant factor against cancer present in the serum of some people, or at least some ability to defend against malignant growth. He regrets that a similar letter from him some years ago raised no interest. His letter in May surely interested our department, where we have worked for some years on this problem. We found in 1946 that some rats inoculated with Walker's rat carcinoma remained immune against any further grafting, even if this was done repeatedly. We kept these immune animals and later found that all of them had immensely enlarged musk, or scent, glands. When we removed these glands the immunity disappeared, and grafting was again successful. In some of these formerly immune animals the cancer started to grow spontaneously, which shows that some cancer cells from former grafting were present in a sleeping stage.

If we implanted an enlarged gland from an immune animal into an ordinary rat with a cancerous growth the growth was stopped and the tumour disappeared. Since these findings we have tried to get from the musk glands the substance responsible for this immunity. Till now we have not been successful, though we were able to describe some substances with a partial influence on the growth of cancer. As material we used dried musk glands of Canadian beaver and similar glands of other water rodents which are suitable because they are a compact gland. We have thought of the possibility that the musk glands or sebaceous glands are an organ capable of eliminating some toxic substances which lead to cancer growth. We are not pathologists, but we think it would be worth while to observe the preputial and sebaceous glands in patients suffering with cancer, because these glands are analogous to the musk glands of rodents. Some of our findings have been published in Czech papers, and the original publication was in *Comptes rendus des séances de la Société de biologie et de ses filiales* (1948, **142**, 109). If anybody is interested in this question I should be pleased to give any required details.

I apologize for the delay in sending this letter, but the *British Medical Journal* takes a long time to reach me.—I am, etc.,

School of Medicine, Brno University, Brno, Czechoslovakia. JIRI STEFL.

Chelation

SIR,—Your annotation on chelation (*Journal*, December 19, 1953, p. 1365) suggests that one of the characteristic properties of chelating agents is the formation of water-soluble complexes with metals. Such an impression is quite erroneous. It is true of some chelators—for example, ethylene diamine tetracetic acid[1]—but the great majority of metal-chelate complexes are only sparingly soluble in water.[2 3 4] For this very reason, many chelating agents have been used in analytical chemistry for the estimation of metals.

Perhaps the oldest clinical example of a chelating agent is oxine (8-hydroxyquinoline), which, in the form of "chinosol," has been used for over 50 years as a surface antibacterial, and also as a fungicide and chemical contraceptive. The mode of action of oxine has been extensively studied by Albert *et al.*,[5] who have suggested that its antibacterial properties might be dependent upon it depriving organisms of essential trace elements. Whilst this may be so with some bacteria, with others the actual toxic agent is probably a metal-oxine complex. In highly purified media, for example, oxine has been found inactive, but its toxicity can be restored by adding traces of heavy metals.[6] A more recent clinical example of a chelating agent is of course B.A.L., which, by virtue of its ability to bind arsenic and certain metals, has found wide medical application in cases of poisoning by these substances.

We have tested the toxicity of a number of chelating agents for mammalian spermatozoa in this department. Sodium diethyldithiocarbamate, nitroso-naphthol, and ethyl potassium xanthate were found to be much more toxic to human spermatozoa than was oxine, and these newer chelating agents may be valuable as chemical contraceptives. Interestingly enough, in view of Albert's finding with bacteria, the spermicidal efficacy of oxine and some of the other chelating agents was greatly improved by traces of copper and other heavy metals.—I am, etc.,

Sydney, Australia. I. G. WHITE.

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3 Yoe, J. H., and Sarver, L. A. (1941). Ibid., p. 105. London.
4 Albert, A., and Gledhill, W. S. (1947). *Biochem. J.*, **41**, 529.
5 *Brit. J. exp. Path.*, 1947, **28**, 69.
6 Rubbo, S. D., *et al.* (1950). Ibid., **31**, 425.

Periodic Medical Examination

SIR,—As a member of the lay public whose opinions on medical matters you somewhat sweepingly dismiss as "usually ill-informed and singularly opinionated," I think your annotation, "Periodic Medical Examination" (*Journal*, November 6, p. 109), is in no small danger of incurring the latter of those epithets itself. While you admit that medical opinion is sharply divided on the desirability of periodic overhaul, the arguments with which you support your own negative attitude seem to me somewhat thin, and you do scant justice to the opposite views. You cite the cases of two men who died of carcinoma of the colon to show the danger of the false sense of security that a "negative" overhaul may engender. But it is notorious that carcinoma can do irremediable damage before it becomes clinically demonstrable. Your argument implies that, because one type of lesion cannot be clinically demonstrated by an exhaustive examination, therefore it is not worth while making any such examination unless the patient has a symptom of illness. But this is to neglect some weighty evidence that human beings possess a compensating mechanism the power of which to mask major disease can be staggering. Scott Williamson and Pearse[1] found that among 1,530 individuals investigated there were 902 with an "almost assertive sense of well-being." Yet among major disorders discovered of which the sufferers in this group knew nothing were heart disease, kidney disorder, tuberculosis, bronchiectasis, gastric ulcer, pernicious anaemia, and high and low blood pressure. One young man of 21, who wanted to be a boxing and gymnastic champion, actively pursuing his interests, was sustaining valvular disease of the heart, nephritis, a blood pressure of 230, and an almost solid albuminuria, while he "never felt fitter in his life." Treatment was effective in removing all his disorders except the valvular one. The authors observe that in a sense of well-being there is this fundamental danger—it deceives the individual and, in cases of this kind, the casual observer.[2]

Your view that the public should seek advice for any symptom of illness seems to me wholly to ignore the evidence accumulated by the Pioneer Health Centre. A disturbingly high proportion of people who felt perfectly fit were found to be suffering from serious disorders. The investigation made while they felt fit enabled many to have their conditions treated before the ultimate breakdown of compensation and the consequent shortening of the expectation of life. Do you advocate visits to the dental surgeon only when there is a pain in a tooth? Caries and major disease of the teeth can go very far before a symptom

emerges. It is true that regular visits to the dental surgeon will not guarantee dental health. But they can prolong dental life and stave off general dental collapse in many a mouth, and in not a few protect the health that nature has given their owners. I fail to see that this situation does not apply to any other system of the body–mind complex than the teeth. I hope the public will demand with growing insistence the provision of routine medical overhaul, and that the profession, instead of opposing it, will welcome an opportunity of establishing a doctor–patient relationship that will enable the former to gain a wider appreciation of the whole constitution and personality of the latter than can be gained by short interviews on specific symptoms in crowded surgeries.—I am, etc.,

Sherborne. H. BOX.

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1 *Biologists in Search of Material: An Interim Report on the Work of the Pioneer Health Centre, Peckham*, 1947, p. 82. Faber, London.
2 Ibid., 1947, p. 83. Faber, London

SIR,—In referring to the "cult of periodic medical overhaul" (*Journal*, November 6, p. 1095) and to Sir Adolphe Abrahams's "pungent and lucid criticism" of this practice, neither your annotator nor Sir Adolphe applied what is surely an appropriate test—namely, the measure of success. Both quoted selected failures, but how would medicine in general look if subjected to this unsatisfactory line of criticism? It is better to ask whether such preventive measures, after taking the cost into account, result in better husbandry of life. Is sufficient illness prevented, are sufficient lives saved, to justify the procedure and its cost? This economic test may be applied to each item of a preventive examination separately, and, although it may "go without saying that a *full* overhaul must include examination of the rectum" (my italics), it in no way follows that routine rectal examination would be economically rewarding or desirable for health supervision.

I agree with Sir Adolphe when he says preoccupation with disease may not provide the best *milieu* for health-mindedness; I would go further and say it does not. I have in the last year or so listened to three learned societies discussing the management of hypertension. Rare conditions such as phaeochromocytoma found a place in each discussion, but the effective prevention of cardiovascular disease by weight supervision, to which I have referred elsewhere,[1 2] was not so much as mentioned. Early management has greater chance of success than late management and should not be excluded from discussion because of doctors' preoccupation with late manifestation of disorder. If this is the necessary heritage of our training, the training needs to be extended to lay more emphasis on preventive techniques and their development. Life insurance companies might, for example, not only improve their own business, but postpone many deaths at present occurring in middle age, if they made more use of fat callipers to distinguish weight due to fat from weight due to muscle. Athletes with less than average fat would be among those chiefly benefiting by better premiums, and I understand some companies already vary their premiums according to periodic medical reports. The recent publication of separate age, height, and weight tables for each somatotype[3] is a valuable aid to current thought and technique, but, if preventive medicine is to succeed in the future in postponing the effects of cardiovascular disorder, periodic medical examination cannot be set aside.—I am, etc.,

Oxford. R. W. PARNELL.

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1 *Lancet*, 1952, 1, 105.
2 *Med. Press*, 1954, 231, 567.
3 Sheldon, W. H., *et al.* (1954). *Atlas of Men*. Harper, New York.

SIR,—I found the annotation on periodic medical examination (*Journal*, November 6, p. 1095) most interesting, although it approaches the subject from a curative rather than a preventive point of view. The fact is that periodic medical examination is now available to every pregnant woman and all children up to the age of 15 years, and I do not think the public or the medical profession are deluded if they recognize that these examinations by the public health service have contributed to improved health and lowered mortality in children and their mothers. It seems to me that, as far as resources permit, the scope of preventive medicine should be extended to other age groups, the periodic medical examination being regarded as an extra health measure rather than as an alternative to consulting the general practitioner about symptoms, and the time allowed being an average of five minutes as for school-children. If this service was practicable at all and could take over when the adolescent leaves school the chronic diseases discovered by Baker *et al.*[1] could at least be observed in their incipient stages if not avoided altogether.

The case you quote of the man whose normal barium enema skiagram gave him a false sense of security is surely not an argument against medical examination, only against available diagnostic technique; the lesson to be learned from the case of the doctor with electrocardiogram evidence of bundle branch block must surely be that the sick doctor becomes "a singularly opinionated layman," and should be told only reassuring findings—without either terrifying him or making light of his complaints. Routine chest *x* ray may be the most essential ancillary investigation necessary from a public health point of view.—I am, etc.,

Enfield, Middlesex. C. M. SMALL.

REFERENCE

1 *Sth. med. J. (Bgham, Ala.)*, 1953, **46**, 984.

R.M.B.F. Christmas Gifts

SIR,—The Royal Medical Benevolent Fund hopes to post the Christmas gifts to its beneficiaries in the very near future. May I remind your readers who have not already contributed to send donations marked "Christmas Gifts" to the Royal Medical Benevolent Fund, 1, Balliol House, Manor Fields, Putney, London, S.W.15, as soon as possible?—I am, etc.,

London, S.W.15. FRANK JULER,
Honorary Treasurer,
Royal Medical Benevolent Fund.

POINTS FROM LETTERS

The War Memorial

Mr. E. WATSON-WILLIAMS (Bristol) writes: Would the sculptor responsible for the statue of Machaon . . . explain why the hero is shown wounded in the *thigh* (*Journal*, November 6, pp. 1098–9)? Homer is explicit: Machaon was wounded in the right shoulder (*Iliad* XI, 507).

Dental Anaesthetics for Children

Dr. F. W. B. GREAVES (Haberfield, N.S.W., Australia) writes: It is surprising that in these enlightened days anyone would contemplate even the most minor surgical procedure in the mouth of an unconscious patient, either adult or child, without provision for a continuous anaesthetic, and an efficient suction apparatus with the head in the dependent position and the fauces packed lightly with gauze. To even the most expert, delay is as unpredictable as it is unavoidable from the caprice of that elusive tooth crown which chooses to snap off and seek seclusion somewhere in the anatomy of the upper air passages, or maybe from the difficult stump from the carious tooth. Surely the "head hanging" (Rose) position and the hazard of inhalation of foreign matter are worth keeping in mind.

Pain on Swallowing

Dr. ERIC J. TRIMMER (Oxhey, Herts) writes: This is often a distressing symptom and is not always helped by the method recommended in Dr. J. Kohn's letter (*Journal*, November 6, p. 1105). Likewise local analgesic lozenges are also very disappointing in their action. The most constantly acting measure that I have found is simply to allow one soluble aspirin tablet to dissolve in the mouth about 10 minutes before eating. This provides an astonishing freedom from pain for about half an hour.

Obituary

H. M. TRAQUAIR, M.D., F.R.C.S.Ed.

Dr. H. M. Traquair, consulting ophthalmic surgeon to Edinburgh Royal Infirmary, died at Edinburgh on November 14, aged 79, after a long and trying period of ill-health.

Harry Moss Traquair was born at Edinburgh on September 13, 1875. He was the younger son of the late R. H. Traquair, F.R.S., and his mother was a distinguished artist. He was educated at Edinburgh Academy and at Edinburgh University, taking the degrees of M.B., C.M. in 1901, with first-class honours, and the D.P.H. in the following year. He worked also at the University of Halle, and for reasons of health went for a time to South Africa as a general practitioner.

[Drummond Young, Edinburgh

Traquair returned to Edinburgh to devote himself to ophthalmology. He proceeded to the M.D. in 1903 and was elected F.R.C.S.Ed. in 1904. The usual series of appointments followed, and at the end of his active hospital life he was senior ophthalmic surgeon to the Royal Infirmary and senior lecturer in the university. He was President of the Royal College of Surgeons of Edinburgh from 1939 to 1941, and of the Ophthalmological Society of the United Kingdom in 1943–4. In addition he was a member of many foreign ophthalmological societies and of the council of the Faculty of Ophthalmologists.

Such a record, with private practice in addition, might well be supposed to indicate a full and complete life, but Traquair's mental gifts and energy were so outstanding that he was able to add to it achievements in research that have rarely been surpassed in his own field. He began his work as an ophthalmologist at the time when the late Sir George A. Berry and Dr. A. H. H. Sinclair had already shown the great importance of the investigation of the visual fields, and he continued their work with immense determination and tireless energy. Before long he had become a world authority, and probably the leading one, on the subject. The sixth edition of his classic book, *Clinical Perimetry*, was published in 1949. A complete list of his other publications is too long to detail, but mention should be made of another book, *Clinical Ophthalmology for Practitioners and Students*, published in 1948. He was awarded the Middlemore Prize in 1920, the Nettleship Medal in 1922, the Doyne Memorial Medal in 1923, and the Mackenzie Memorial Medal in 1939. He served as a vice-president of the Section of Ophthalmology at the Annual Meetings of the B.M.A. in 1921, 1927, and 1935.

A very important part of his research was concerned with the diagnosis of affections of the visual pathways at the base of the skull, and this work brought him into intimate touch with the then relatively new subject of surgical neurology. In this connexion Professor Norman M. Dott writes: "I have abundant cause to salute Dr. Traquair with reverence and gratitude. Returning from a period of training with Dr. Harvey Cushing I found him a powerful friend and promoter of modern surgical neurology. His practical help in investigation and in the management of patients and his constant inspiration and encouragement were generously available; his wise and powerful influence in the councils of the Edinburgh school made progress in surgical neurology possible."

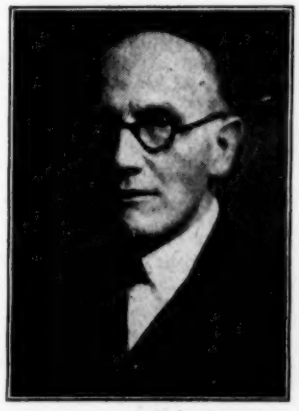
Traquair was due to retire from the staff of the Edinburgh Royal Infirmary in 1940, but since his successor was on war service he was asked to continue. This he did willingly, and when he eventually retired in 1943 the managers of the infirmary, appointing him to the post of consulting surgeon, took recognition of the prestige which the infirmary had gained from his work and recorded their sincere thanks for the many years he had given of skilful and devoted service.

In 1906 he married Miss Beatrix Nairn, and is survived by her, a daughter, and a son, who is an orthopaedic surgeon.

E. H. C. writes: This brief and incomplete account of Traquair's professional life must serve to show the scope and quality of his attainments, but it is important to try to describe the man himself, since he was in the opinion of his Edinburgh colleagues one of the most brilliant intellects of his day in the medical school. He had a highly developed critical faculty and capacity for seeing relationships combined with a fresh and very original outlook. With these gifts, very accurate powers of observation, and a retentive memory, he was well equipped for the career of his choice. He once told me that in his boyhood he had determined, if possible, to attain high position in medicine in Edinburgh, and amply was this ambition realized. He was widely read in general literature, a good linguist, an interesting and entertaining companion, and kindly and helpful to junior colleagues.

Sir ROBERT STANTON WOODS, M.D., F.R.C.P.

We regret to announce the death on November 18 of Sir Robert Stanton Woods. He was a leading authority in this country on physical medicine, and indeed a pioneer in that subject which, during his professional career, he had seen grow from small beginnings into full recognition and authority. For a generation he had been a very active figure on the staff of the London Hospital and was consulting physician to the hospital at the time of his death.



[Walter Stoneman

Robert Stanton Woods was born on February 10, 1877, the son of Robert Woods, J.P., of Stewartstown, Co. Tyrone. He was educated at the Royal School, Dungannon, from which he went on to Queen's University, Belfast, with a classical scholarship. Coming to London, he completed his medical training at University College and at the London Hospital, qualifying in 1904 and afterwards holding numerous resident posts at his own hospital. He proceeded M.D. London in 1909, and in the following year became a Member, and in 1932 a Fellow, of the Royal College of Physicians. During the 1914–18 war

he served as a major in the R.A.M.C. and was mentioned in dispatches from France in 1919.

Woods completed his medical studies in Stockholm and Vienna, where he made himself acquainted with the methods of physical medicine then being enthusiastically pursued in those schools. Elected to the staff of the London Hospital, he was given charge of the department of physical medicine in 1911. The London Hospital had always been a pioneer in this field. It was there that Finsen light was first used in this country at the beginning of this century. Woods built up the department and kept himself fully abreast of all the work which was being so vigorously pursued in many quarters in those years. Later, in 1936, he inaugurated a school of physical medicine at the London.

His name came prominently before the public when at the end of 1928 he was called in as one of the ten medical men in attendance on King George V in his grave illness, which culminated in emphysema. Lord Dawson summoned him and Dr. F. D. Howitt, both of them specialists in physical medicine, to administer ultra-violet ray therapy with the mercury lamp in order to stimulate the vitality of the tissues and supplement other treatment. This assisted the King's recovery, and as a mark of royal appreciation of his services Woods received a knighthood in 1929.

Stanton Woods wrote comparatively little—only a few papers on various aspects of physical medicine and education in that specialty are attached to his name—but he was a frequent participant in medical discussions, and he lost no opportunity of presenting—as he could do very forcibly—the claims of physical medicine. He also brought home to local authorities and industrial concerns the importance of physical training. In 1932 he was president of the Section of Physical Medicine of the Royal Society of Medicine. His presidential address was on "Osteopathy: An Investigation." He had been a prominent figure as a witness in the famous inquiry by a committee of the House of Lords into the claims of osteopaths for registration. In 1936 when the International Congress of Physical Medicine was held in London Stanton Woods was an obvious choice as president, and from that year until 1946 he was consulting adviser to the Ministry of Health on matters connected with physical medicine and education. His reputation extended beyond this country, and he was made an Honorary Fellow of the American Academy of Physical Medicine.

He married in 1917 Mrs. Violet Liebert, widow of an officer of the 7th Hussars, who survives him with one daughter. A son died on active service during the second world war.

We are indebted to Sir ALUN ROWLANDS for the following appreciation: Robert Stanton Woods qualified at the time when great strides were being made in that branch of therapeutics which has since been designated as physical medicine. Already massage was being more widely applied as a mode of treatment, and Lucas-Championnière in France (1843–1913) was advocating its use in the treatment and rehabilitation of fractures. Head and Sherren had just published their work on peripheral nerve injuries and pointed out the frequent association of fractures and nerve injuries. Tyrnauer baths had been instituted at the London Hospital in 1909, and electrical treatment, *x*-ray diagnosis, and light treatment for skin conditions, all in their initial stages, were grouped together, and several medical officers were partly responsible. Dr. E. R. Morton was medical officer in charge of the electrical department from 1903 to 1910. Dr. J. H. Sequeira was then doing some work on the *x*-ray treatment of skin conditions. The four technicians who worked in the departments about that time developed *x*-ray dermatitis and died subsequently from superimposed cutaneous carcinoma. In 1910 the London Hospital authorities decided to amalgamate the electrical, massage, and Tyrnauer bath departments and appoint one medical officer in charge. Late in 1909 an *x*-ray department, which was mainly diagnostic, had been placed in charge of the newly appointed radiologist, Dr. Gilbert Scott. The *x*-ray treatment of cutaneous conditions still remained under the care of Dr. J. H. Sequeira. In March, 1910, Woods was appointed medical officer in charge of the electrical department, and a year later physician in charge of the electrical and physical treatment department. In 1930 he was made physician in charge of the department of physical medicine. The titles applied to these appointments mark the development of the specialty. In 1936 the new department of physical medicine was opened by the late Duke of Kent, and the school of physiotherapy was instituted.

For many years Stanton Woods gave devoted service to his departments at the London Hospital. When patients were referred to him he took a careful history and made a thorough clinical examination, and reviewed the progress that had already been made, all his observations being scrupulously recorded. His medical and surgical colleagues were quick to appreciate and acknowledge the help that his departments were able to give in the treatment of their patients, so the work done by Woods quickly increased. He was most attentive to the smallest detail in the treatment of his cases, for instance, any change in splintage, the degree and frequency of passive and active movements, the progress of nerve injuries, and the advisability of, and the appropriate time to consider, any further surgical aid. He always stressed the detailed attention necessary to get patients completely restored to health and returned to work as soon as possible. When the Workmen's Compensation Act (1925) came into force, Woods was soon recognized by the representatives of both employers and employees as an ideal expert witness, his evidence being always thorough, fair, and judicial. Two great wars, with their tragic aftermath of physical injuries, have shown the great need for physical aids in the rehabilitation of the injured, and Woods played a great part in the application of the principles of physical medicine to the treatment of the wounded and disabled. He was a very loyal friend and colleague, and gave a long and distinguished service to his hospital and his patients. Very many will mourn his departure.

D. C. L. FITZWILLIAMS, C.M.G., M.D., Ch.M. F.R.C.S.

His many friends will be sad to hear of the death of Mr. Duncan Fitzwilliams, which took place on November 18 at St. Mary's Hospital, with which he had been associated for 45 years as surgeon and consulting surgeon. For the past two or three years he had been in indifferent health, but the end came rather suddenly. He was 75 years of age.

Duncan Campbell Lloyd Fitzwilliams was born on December 31, 1878, the son of Charles H. L. Fitzwilliams, J.P., of Newcastle Emlyn, Cardiganshire. He received his medical education at Edinburgh University, where he achieved distinction by gaining the Lechie-Mactier and the Goodsir Memorial Fellowships. He graduated M.B., Ch.B. in 1902, and in 1904 his fellow students elected him president of the famous and old-established Royal Medical Society. He also gained fame as an outstanding heavyweight boxer. After qualification he volunteered for service in the R.A.M.C. in the South African war, being awarded the Queen's Medal with four clasps. He returned to Edinburgh and gained the gold medal at the M.D. and high commendation at the Ch.M. examinations. After holding resident posts at the Royal

Infirmary, Edinburgh, and the Edinburgh City Hospital he was appointed demonstrator of anatomy at the New School of the Royal College of Surgeons of Edinburgh, whose Fellowship he obtained in 1905. He then came to London, and after holding the posts of house-surgeon and casualty officer at the Hospital for Sick Children in Great Ormond Street he was appointed demonstrator of anatomy at King's College and clinical assistant to the surgical out-patients departments of the West London Hospital and the Hospital for Sick Children. In 1906 he became F.R.C.S. England. His brilliant academic distinctions received full recognition in 1909 when he was elected surgeon to out-patients at St. Mary's Hospital, Paddington. From that time his name soon became widely known among the surgical world. He was appointed to the surgical staff of Paddington Green Children's Hospital, and later he also became surgeon to the Mount Vernon Hospital and Radium Institute for Cancer. Among the other hospitals to which he was attached at one time or another were the Margaret Street Hospital for Diseases of the Chest, and the Dorking, Hanwell, Hayes, and Barnet Cottage Hospitals. A keen Freemason, he attained high rank in Grand Lodge, and for many years served on the surgical staff of the Royal Masonic Hospital. For a period during the second world war he resided at that hospital ready to deal with any emergency.

[*Elliott and Fry*

In the 1914–18 war Fitzwilliams served for a time with the 1st City of London Field Ambulance. Towards the end of the war he had some remarkable experiences when acting as consulting surgeon to the North Russian Expeditionary Force. Twice mentioned in dispatches, he was created C.M.G. in 1919, and held a number of Russian and Rumanian crown honours, besides being a Chevalier of the Legion of Honour. He was also a Knight of the Order of St. John of Jerusalem.

As a surgeon "Fitz," as he was commonly called by nearly everyone who knew him, was courageous and enterprising. He had an independent mind with an original outlook untrammelled by tradition. An enthusiastic exponent in the use of radium in the treatment of malignant disease, he wrote much to advocate and expand this method of treatment, including a book entitled *Radium and Cancer*, published in 1930. He was a ready lecturer with a colloquial style of speaking, and he seemed to find writing easy, for in addition to the book already mentioned he published several others, of which the chief were two very useful monographs dealing respectively with diseases of the tongue and of the breast. He was popular with the students and with young people generally, probably because he retained all through his life a certain youthful enthusiasm and eagerness of outlook. His summertime parties at his house on Monkey Island, on a beautiful reach of the Thames at Bray, were much looked forward to and enjoyed by the students.

As a man Fitzwilliams was a commanding presence, being six foot four inches in height and broad in proportion. He was a good companion, a loyal colleague, and a faithful friend. He often added liveliness to the discussions at many medical societies, and served a term as president of the Harveian Society and of the West London Medico-Chirurgical Society, as well as being president of the Clinical Section of the Royal Society of Medicine. He was also at one time Master of the Society of Apothecaries, and was much interested in its history. In later years he wrote many articles on various aspects of the history of medicine, and on one occasion he even took up the cudgels in defence of Sir Everard Home. After his retirement from the active staff of his hospitals, Mr. Fitzwilliams went to live in Jersey, where he continued to do a certain amount of surgery. When necessity demanded it he came to London for surgical treatment himself, and, though he was able to return to Jersey, he never completely regained his former state of health.

Mr. Fitzwilliams was twice married. By his first wife, who died in 1919, he had two sons and three daughters. His second wife survives him, and to her and to his children we tender our sympathy.

A. J. BALLANTYNE, M.D., LL.D., F.R.F.P.S.

With the death on November 10 of Professor A. J. Ballantyne, emeritus professor of ophthalmology in the University of Glasgow, Scotland has lost another leading ophthalmologist.

Arthur James Ballantyne, the son of a Glasgow merchant, was born in 1876, the youngest member of a large and, as events proved, brilliant family. He was educated at Garnethill School—it was characteristic of him to name it a board school in a book of reference—and at Glasgow University, where he graduated M.B., Ch.B. in 1898. Three years later he proceeded to the M.D. with a thesis on the contusion injuries of the eyeball, illustrated by his own drawings. He became a Fellow of the Royal Faculty of Physicians and Surgeons of Glasgow in 1906. After graduating he served a year as resident in medical and surgical wards at the Glasgow Royal Infirmary and a year as house-surgeon at the Glasgow Eye Infirmary, where his colleague was George Coats, afterwards curator and surgeon at Moorfields. With Coats he spent a *Wanderjahr* at the great Viennese school of ophthalmology, and while there he passed much time at the opera and at concerts.

On his return to Glasgow Ballantyne was appointed a junior on the staff of the Glasgow Eye Infirmary, but, unlike most of his generation, he did not enter general practice as a means of livelihood while becoming established in specialist practice. From 1909 until 1914 he was professor of physiology at the Anderson College of Medicine, but even with that financial aid his early years must have been lean ones. This experience probably accounted for his view, often expressed to his juniors, that, in the end, a hard beginning was the best apprenticeship that could be served to consultant practice. In 1909 he was appointed surgeon to the Glasgow Eye Infirmary at the then unusually early age of 33. Throughout this entire period he kept his connexion with the medical wards of Glasgow Royal Infirmary, and particularly with those of Dr. John Cowan. It was there that he obtained a grounding in the medical aspects of ophthalmology and thus laid the foundation for the work of his later years. As surgeon to the Glasgow Eye Infirmary he was called upon to teach both undergraduates and postgraduates, and was successively lecturer in ophthalmology at St. Mungo's

College and at Anderson's College, until in 1920 he was appointed to the lectureship in ophthalmology at Glasgow University, to the post first held by William Mackenzie, one of the founders of the Glasgow Eye Infirmary. During the first world war he served in a general hospital in Salonika as ophthalmic specialist.

The years after the war were spent in a busy and successful consultant practice. He was a popular teacher, a dexterous yet careful operator, an excellent clinician, and a scrupulous observer and recorder of all his findings. When on the point of retiring from the Eye Infirmary he was appointed in 1935 the first occupant of the newly created Tennent chair of ophthalmology at Glasgow University, and a director of the Tennent Institute for Research and Postgraduate Teaching of Ophthalmology at the Western Infirmary. This new appointment gave him the opportunity, the material, and the facilities for carrying out work which he had long been planning on the co-relation of the ophthalmoscopic appearances with the pathological alterations in the choroid and retina. He curtailed his private practice severely and devoted the major part of his time to academic pursuits in the new institute. During the next ten years he produced a series of papers on the vascular changes of diabetes and hypertension which illuminated this aspect of ophthalmology and constituted his greatest work. His drawings and paintings of the fundus were those of an artist. Besides possessing the ability to record in word and picture the changes taking place in the fundi, he had the patience to wait until the fundus came to pathological examination before completing his records of individual cases. In addition, he devised valuable new methods of preparing specimens, and these helped to emphasize the accuracy of his observations. The advent in Glasgow in 1938 of Professor Arnold Loewenstein, an exile from Czechoslovakia, provided a partnership which was stimulating both to the work of the department and to Ballantyne's own researches on blood vessels.

Throughout his life Ballantyne published some fifty papers, alone or in collaboration: their content was varied, as is shown by such titles as "Congenital Anomalies," "Heterophoria," "Squint Operations," but in his latter years he wrote chiefly on the pathology of lesions seen on fundus examination. His original work was recognized by the award in 1942 of the Mackenzie Memorial Medal, for the institution of which he himself was very largely responsible, and by the Nettleship Prize of the Ophthalmological Society of the United Kingdom in 1950. He was called upon to deliver the Doyne Memorial Lecture at the Oxford Ophthalmological Congress in 1946 and the Montgomery Lectures in Dublin in 1943. He also lectured in Basle and in N. America on vascular changes in the retina. At different times he was president of the Ophthalmological Society of the United Kingdom, of the Section of Ophthalmology of the Royal Society of Medicine, of the Section of Ophthalmology at the Annual Meeting of the British Medical Association in 1935, and of the Scottish Ophthalmological Club. He was an honorary member of the Chicago and Irish Ophthalmological Societies. On his retirement from the professorship at Glasgow in 1941 the University conferred on him the honorary degree of LL.D. and the title of professor emeritus. He also received the honorary degree of D.Sc. of the Roanoke College, Virginia.

Ballantyne had many cultural interests outside his professional work. He was deeply fond of music and seldom missed a performance of the Scottish Orchestra or of the Chamber Music Society. He was keenly interested in art, and, although his own painting was medical and representational, his artistic tastes were seen in the decoration of his own home, and in the colour work which he did with a cinecamera. He served on the council of the Glasgow Institute for Fine Arts for some years, and was on the hanging committee. Always a quiet man, with a dry sense of humour, slow to show feelings in any circumstances, he was profoundly changed by the tragic and premature death of his wife in 1928, although he bore the loss with a stoical outward calm and without any interruption of his daily tasks. He became more devoted to his work, had fewer outside social contacts, and was much more driven into himself. Careful in little matters, he had a generosity and charitableness which were freely at the call of any good cause. Though slow to anger, he could reprove with devastating effect by a quiet word those who deviated from the high professional code which he set himself. His retirement from the chair of ophthalmology made little difference to his mode of life. He still carried on his work at the Tennent Institute, and his publications continued to appear. His latter years were devoted to the production of a book on the pathology of fundus conditions. It was, indeed, just a few days before he died that he completed a sixth revision of the text of the manuscript (it was characteristic that he should consider so many revisions necessary). By his death ophthalmology has lost an indefatigable worker, and the school of ophthalmology at Glasgow a much respected colleague. Critical in nature, somewhat hard on his juniors as a senior, he never demanded more than he could perform himself. He set a standard of work that few could attain.

C. G. L. WOLF, M.D.

Dr. C. G. L. Wolf, honorary consulting biochemist to the United Cambridge Hospitals, died on November 9 at his home in Cambridge three days after his 82nd birthday. He had been in poor health for some time.

Charles George Lewis Wolf was born at Niagara Falls, Canada, the son of Joseph and Isobel Wolf. From the University of Manitoba, where he was first medallist in natural sciences in 1890, he went on to McGill University to study medicine, graduating M.D., C.M. in 1894. After a short period as a teacher in Canada he came to Europe to continue the study of organic chemistry at Cambridge and Würzburg Universities. Returning to North America, he was demonstrator in chemistry at the Medical College of McGill University until 1899 and then moved to Cornell University Medical College in New York, where he was first instructor and then assistant professor and head of the department of physiological chemistry from 1899 to 1911. At the outbreak of the first world war he joined the R.A.M.C. and was in charge of a base hygiene laboratory from 1915 to 1917, being twice mentioned in dispatches. Towards the end of the war he was appointed a member of the Bacteriological Committee of the Medical Research Committee (the forerunner of the Medical Research Council). For some time before this he had been working with the late Sir Frederick Gowland Hopkins in

Cambridge, and in 1921 he was appointed honorary biochemist to Addenbrooke's Hospital. He retired from this post in 1937 and was then appointed to the honorary consultant staff of the hospital. He was the author of many articles on biochemical and physiological subjects and edited the chemical section of Sahli's *Clinical Diagnosis*. Being a skilful and experienced laboratory worker and possessing an original turn of mind, he always took great pleasure and much trouble in helping any young man who sought his advice about scientific problems in his own field of work.

In later life Dr. Wolf took an active part in local government, and was a member of the Cambridge Borough Council from 1936 to 1946, serving on many committees and being chairman of the public health committee from 1945 to 1946. He was also a member of the Cambridge County Council until 1946, taking a particular interest in the work of the education and health committees.

Dr. Wolf married his cousin, Josephine Rebecca Tallerman, in 1910. She died five years ago, and there were no children of the marriage.

REGINALD WORTH, O.B.E., M.B.

Dr. Reginald Worth, medical superintendent of Springfield Mental Hospital from 1912 to 1939, died on November 15, aged 81.

Reginald Worth was born at Anderton, Cornwall, on April 8, 1873, the son of Dr. E. J. Worth. From Epsom College he went on to study medicine at St. Mary's Hospital, qualifying in 1896. Five years later he graduated M.B., B.S. at Durham University. After holding an appointment as assistant house-surgeon at Cardiff Royal Infirmary he decided to enter the mental hospital service and for a time was a clinical assistant at the West Riding Asylum at Wakefield. Early in this century he was appointed junior assistant medical officer at Springfield (then called the Middlesex County Asylum) and in due course he became senior M.O. and then medical superintendent. During the first world war he served as a major in the R.A.M.C. and was appointed O.B.E. in 1919.

Worth was a most efficient superintendent and became very well known in the mental hospital world. For some years he was lecturer in psychological medicine at the Westminster Hospital, and he was also a member of the General Nursing Council. Having been honorary general secretary of the Royal Medico-Psychological Association, he was elected its president in 1935. He retired from the post of medical superintendent of Springfield Hospital in 1939, but returned to work during the last war as temporary medical superintendent of the City of London Mental Hospital, Dartford. In recent years he had lived within sight of the Solent, first at Hill Head and later at Milford-on-Sea.

We are indebted to Dr. H. C. BECCLE for the following appreciation : Although not entirely unexpected, the death of "Reggie" Worth, as he was affectionately known to all those privileged to work with him, brought to me an acute sense of personal bereavement. He was a psychiatrist of the older "orthodox" school, who, although not preoccupied with diagnostic labels, displayed in his clinical work sound common sense and a penetrating judgment. It is safe to say that he was literally worshipped by his patients, most of whom he knew by name, a considerable feat in a large mental hospital. He also commanded the respect of all who came under his dominion.

During his long and distinguished career at Springfield, which brought him a well-merited civil distinction and later the high office of presidency of the Royal Medico-Psychological Association, he was instrumental in bringing about many geographical and clinical improvements. Largely his life was devoted to one purpose and one purpose only, that of enhancing the welfare of his patients. To this end he brought a shrewd intellect, a wealth of good-humoured patience, mature tolerance, and a whole host of new ideas. Without being hearty, his infectious optimism had a tonic value which far surpassed such therapies as were extant in the early decades of this century. All in all, his leadership was both inspiring and supportive.

Apart from his work, he was a fine sportsman, literally and metaphorically, and a charming and generous host completely free from personal asperities. Thus it was that as the head of a sizable hospital he was able to develop a corporate spirit therein which has never since been equalled. "Reggie" was Springfield, and Springfield was "Reggie," the two words having become virtually synonymous.

He retired in 1939 after forty years of active and busy endeavour, only to return to the psychiatric fold during the war, when he took over the City of London Hospital as temporary medical superintendent. Thereafter, when life should have treated an honourable retirement kindly, he had to face personal and domestic vicissitudes of a tragic character. A happy family life was shattered by the loss of his two younger sons, one in a submarine and the other from illness. This was a devastating blow. His later years were taken up with a long battle against steadily declining health aggravated by inability to drive his car and play his favourite game, golf. Towards the end he bore a considerable load of suffering with great fortitude.

F. H. NIMMO, M.V.O., M.R.C.S., L.R.C.P.

Surgeon Rear-Admiral F. H. Nimmo, who served for some years as medical officer in two Royal yachts, died at his home at Alverstoke, Hampshire, on November 15 at the age of 82.

Frank Hutton Nimmo was born at Oakleigh Park, Hertfordshire, on June 13, 1872. Educated at Mill Hill School, he won a Jeaffreson exhibition to St. Bartholomew's Hospital Medical School in 1890 and qualified M.R.C.S., L.R.C.P. six years later. Immediately after qualification he entered the Royal Navy as a surgeon and served in H.M.S. *Pigmy* during the Boxer rising at the turn of the century and was present at the capture of the Shanhaikwan forts. Later he was surgeon in H.M.S. *Good Hope*.

Nimmo first entered the personal service of the Royal family in 1908, when he was appointed medical officer to H.M. Yacht *Osborne*. Later in the same year he became medical officer to H.M. Yacht *Alexandra*, an appointment he held until the outbreak of war in 1914. He served with the Grand Fleet in H.M.S. *Erin* until 1917 and was present at the Battle of Jutland. On the recommissioning of H.M. Yacht *Alexandra* in 1919 he resumed his duties as medical officer and held the position until 1922, the year in which he was appointed M.V.O. and promoted to surgeon captain. From 1917 to 1919 he was medical officer in charge of the medical division of the R.N. Hospital at Haslar, where he had served earlier in his career from 1905 to 1907. He retired in 1926 with the rank of surgeon rear-admiral. During the last war he was medical officer in charge of the civil defence casualty services for the Gosport district. He married Miss Anne J. R. Mackirdy in 1906 and had two daughters.

Medical Notes in Parliament

Salary Increases in Universities

The increases in university teachers' salaries announced by Mr. BUTLER, Chancellor of the Exchequer, on November 16 "to enable the universities to maintain their standards of recruitment," included the following clinical posts:

Professors.—Salaries ranging from £2,500 to £2,850 a year. These may be increased to £3,100 in certain cases.

Readers.—Salaries within the range of maxima indicated for lecturers.

Lecturers.—Scales rising from £700 a year to maxima ranging from £1,750 to £2,400; or, in the case of lecturers holding posts of special responsibility such as the headship of an independent department, £2,750 a year.

Salaries in preclinical posts would be:

Professors.—From £2,250 to £2,850 a year.

Readers.—Within the maxima indicated for lecturers.

Lecturers.—Scales rising from £700 a year to maxima ranging from £1,450 to £2,050 a year.

In the non-medical posts, grants would be related to basic salaries for professors of £1,900 a year in universities and university colleges. Provision would continue to be made as at present for supplementation, and this would allow for a range of salaries up to £2,850 a year. Readers and senior lecturers will receive salaries with varying maxima up to £1,850 a year; lecturers, scales rising generally from £650 to £1,350 a year; and assistant lecturers, salaries ranging from £550 to £650 a year. An additional allowance of £50, within a maximum of £2,850, would continue to be paid to non-medical staffs of London University.

Mr. Butler also said that the question whether university fees should be increased was under consideration by the committee of vice-chancellors and principals, and if an increase was decided on it would be some time before it could be fully effective.

Geriatric Units

Mr. K. VAUGHAN-MORGAN (Reigate, Con.) on November 15 asked the Minister of Health how many geriatric units were now established; how many beds were provided; and what was the approximate number of patients treated annually. Mr. IAIN MACLEOD informed him that according to the latest available information there were 59 such units for active treatment. These accounted for 20,500 of the total of 53,871 beds normally available for the chronic sick. He had no separate information of the number of patients treated annually in these units, but in the year ended December 31, 1953, there were 101,081 patients treated in beds allocated to the chronic sick.

Leagues of Hospital Friends

Mr. S. AWBERY (Bristol, Central, Lab.) asked the Minister of Health on November 15 if he was aware of the existence of the leagues of hospital friends in many towns and cities, and if he would encourage their formation and equip them to undertake certain tasks in hospitals which would free trained nurses for other and more important duties. Mr. IAIN MACLEOD replied, "Yes." He did everything in his power to encourage the development of leagues of friends and similar voluntary help in hospitals. He hoped that voluntary bodies everywhere would be ready to offer, and hospital authorities to accept, personal service of the kind suggested wherever it could appropriately be done.

Identification of Babies

Lieutenant-Colonel W. H. BROMLEY-DAVENPORT (Knutsford, Con.) asked the Minister of Health on November 15 what were the principal systems adopted in maternity hospitals to ensure that newly born infants were assigned to the right mothers; what advice had been given by his department in this connexion; and what steps had been taken by his department to compare the arrangements in this country with those in overseas countries. Mr. IAIN MACLEOD said the principal method was for a fixed bracelet of adhesive or linen tape bearing the mother's name to be attached to a baby's wrist at birth. He had given consideration to the suggestion of foot-printing, but it appeared to offer no real advantages, and he was informed that methods in general use in other countries did not differ materially from the one he had described.

Miss IRENE WARD (Tynemouth, Con.) on November 19 asked whether, in order to double-check the assignment of newly born babies to the right mothers, a linen tape bearing the mother's name could be attached to each wrist at the baby's birth instead of on only one. Mr. MACLEOD told her that he was arranging for this suggestion to be considered, together with others he had received.

Old-age Pensioners' Food

Dr. CHARLES HILL, Parliamentary Secretary, Ministry of Food, supplied Mr. E. LEATHER (Somerset, South, Con.) on November 15 with figures showing the estimated energy value and nutrient content of old-age pensioners' domestic food consumption (per head per day) over the past four years. He pointed out that for the last full year for which figures were available (1953) consumption of every nutrient except one was higher than in 1951. Mr. BOTTOMLEY (Rochester and Chatham, Lab.) said the Economic Survey showed that for the country as a whole food values were down for last year. Could the Minister explain how they were up in the case of old-age pensioners? Dr. HILL replied that this was a statistical survey used by both Governments, and Labour members should not begin to question its statistical validity just because it did not suit them.

Bogus Doctors

Mr. R. RUSSELL (Wembley, South, Con.) asked the Minister of Health if he would co-operate with the appropriate departments in obtaining greater security against the danger of bogus doctors, many cases of which had been reported in recent months, and if he would accept as a basis the scheme which had recently been sent to him. Mr. IAIN MACLEOD stated on November 18 that the *Medical Register* was publicly available, and he did not think that special measures such as those suggested by Mr. Russell were necessary or practicable.

Prescribing For Private Patients

Mr. JOHN HALL (Wycombe, Con.) on November 22 asked the Minister of Health what was the average cost per person of pharmaceutical medicines prescribed under the Health Service during the past financial year, after allowing for the prescription charge; what was the estimated number of private patients; and what was the estimated cost of extending to private patients the right for which they paid of obtaining medicine on the same basis as National Health Service patients. Miss PAT HORNSBY-SMITH, Parliamentary Secretary, said the answer to the first question was about 19s. Precise estimates to answer the other questions were not available. Nor was the Minister clear what Mr. Hall had in mind when he referred to the right for which private patients paid. Mr. HALL said that if all private patients joined the Health Service the cost, whatever it might be, would have to be borne by the State. Was it the Government's policy to destroy private practice? Miss HORNSBY-SMITH said she could not accept that assumption. The Service was not denied to anyone who chose to accept it.

Mr. HALL asked if the Minister would amend the National Health Service Act, 1946, so as to allow those who elected to become private patients to utilize the other facilities provided by the Act. He was referred to a reply given last July. Mr. HALL then asked if the Government had abandoned the policy announced in *The Right Road for Britain* in 1949, that private patients should be allowed drugs on the same basis as all other contributors to the Health Service. Miss HORNSBY-SMITH replied that the major cost of the Service was paid for out of taxation and not by insurance contributions. The concession asked for would cost

a substantial sum, and there were higher priorities. Dr. EDITH SUMMERSKILL (Fulham, West, Lab.): Would the Parliamentary Secretary agree that if this concession were allowed the Ministry would have to exercise control over the doctors who practise privately? Miss HORNSBY-SMITH: Certainly I would agree.

Mr. HALL asked the Minister of Health what was the evidence referred to in the report of the Committee on General Practice in the Health Service which led the committee to the conclusion that many doctors who wished to use the Service to prescribe for private patients were unwilling to enter into any contract with or to submit to any conditions within the Service. Miss HORNSBY-SMITH stated that the proceedings of the committee were confidential, and the Minister was not in a position to supply any information on this point.

Insecticides on Fruit.—Dr. CHARLES HILL stated on November 15 that he believed oranges were now unaffected by thiourea. A careful watch was being kept on certain other imported fruits, such as pears, for any remains of insecticides.

Air Pollution Report.—The MINISTER OF HOUSING AND LOCAL GOVERNMENT stated on November 16 that he had received the final report of the Beaver Committee on air pollution, and was arranging for its publication without delay.

Merit Awards for Dentists.—The MINISTER OF HEALTH stated on November 18, in answer to Mr. A. SKEFFINGTON (Hayes and Harlington, Lab.), that in England and Wales nine persons, all holding dental qualifications, were in receipt of distinction awards in connexion with the Hospital Service.

Medico-Legal

DEATH FROM ORANGE PITH

The death of a man aged 54 from acute intestinal obstruction due to undigested orange pith was the subject of an inquest at Lewisham held by Mr. W. R. H. Heddy, coroner, on November 5. About a month previously the patient had complained of pains in the stomach, and his doctor prescribed a powder for them. On November 1 the patient's wife was out at work during the day, and when she returned at 6.30 p.m. she found her husband writhing in pain on the settee. He had returned from work about 10.30 a.m. that day. She called the doctor, who came and diagnosed gastritis, prescribing a powder. At 2 a.m. that night the patient was in very great pain, and his wife asked the doctor to attend. That day, November 2, the patient was admitted to hospital at 12.10 p.m. and he died at 5.40 p.m. In reply to a question from the coroner, the patient's wife said that at no time during his illness did her husband associate his symptoms with anything he had swallowed. At the post-mortem examination, Dr. A. C. Hunt, pathologist, found a rolled-up undigested piece of orange 2 in. (5 cm.) in diameter, consisting mainly of pith, firmly impacted in the ileum about 3 ft. (1 m.) above the ileo-caecal junction. The small intestine above the impaction was grossly dilated right up to the stomach by fluid. A verdict of misadventure was returned.

RADON DEATH

The death of a 42-year-old man from malignant disease 20 years after exposure to the radon that caused it was the subject of an inquest held by Mr. K. H. Digby at Southwark on October 15 and 22. In 1934–5 the man worked for a year at the Radium Institute, London, W.1, as a laboratory assistant. His job was to fill radon into capsules. His hands became scaly; he was told his blood count was not up to standard and was advised to give up this work. Subsequently his hands gave him a great deal of trouble and pain, and in 1953 he had a tumour removed from under his right arm. Latterly he had been gravely ill with ulceration of malignant growth in the right axilla and over the adjacent chest. A verdict of misadventure was returned, the man's death being due to acute suppurative bronchopneumonia following radium cancer of the arm.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **November 6** (No. 44) and corresponding week 1953.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	14	1	5	0		20	1	4	0	
Dysentery	468	38	210	3	1	232	35	137	2	1
Encephalitis, acute	3	0		0		2	1	1	0	
Enteric fever:										
Typhoid	2	0	0	0	2	0	0	1	1	
Paratyphoid	14	0	11 (B)	0		11	1	1	0	
Food-poisoning	164	11		2		156	35		0	
Infective enteritis or diarrhoea under 2 years				13	13				15	32
Measles*	4,635	285	572	167	73	742	13	41	9	137
Meningococcal infection	19	1	14	0		30	5	8	2	
Ophthalmia neonatorum	32	3	9	0		21	1	10	1	
Pneumonia†	351	30	143	4		403	25	103	5	
Poliomyelitis, acute:										
Paralytic	36	1	26	2	2	81	5	24	8	11
Non-paralytic	23	1				45	3			
Puerperal fever§	240	55	13	1	1	296	42	16	1	1
Scarlet fever	636	27	155	36	32	1,062	55	189	40	53
Tuberculosis:										
Respiratory	700	82	137	14				147	19	
Non-respiratory	89	2	17	1				24	6	
Whooping-cough	1,953	98	124	19	33	2,096	127	229	40	33

DEATHS in Great Towns	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		0	4		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	5	0	0	1	1	7	1	2	1	3
Influenza	9	0	2	0	1	10	1	0	0	0
Measles		0	1	0	0		0	0	0	0
Meningococcal infection		0	0				1	0		
Pneumonia	160	16	21	3	8	176	23	12	5	5
Poliomyelitis, acute	4	0			1	5	0		1	0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	59	6	9	1	7	93	6	8	2	5
Non-respiratory		0	10	0	1		1	1	0	0
Whooping-cough	3	0	0	0	1	0	0	0	1	0
Deaths 0–1 year	189	22	27	3	6	192	23	35	3	16
Deaths (excluding stillbirths)	4,810	702	518	88	163	4,931	733	533	97	141
LIVE BIRTHS	6,701	1021	794	201	389	7,253	1065	844	198	305
STILLBIRTHS	196	20	23			203	35	28		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

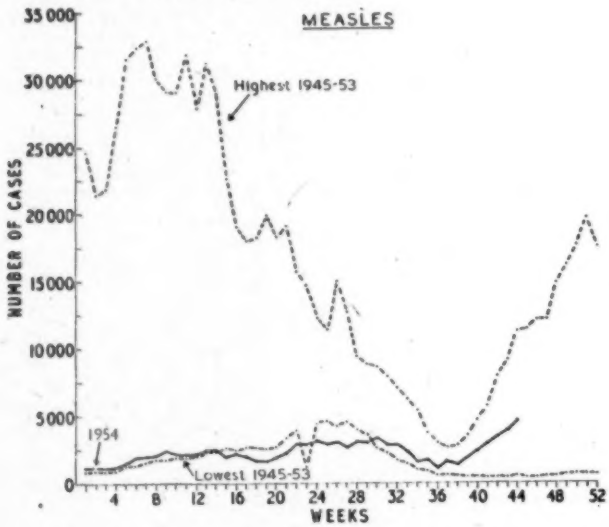
Mild Influenza Outbreaks

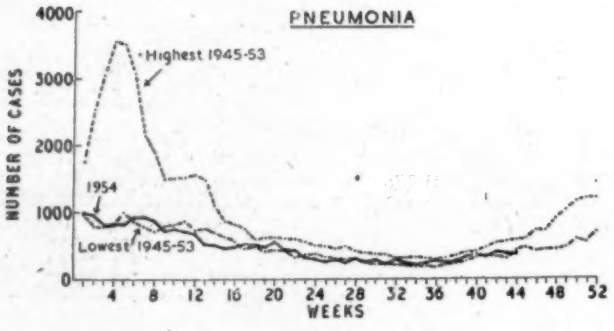
Many outbreaks of mild influenza have been reported in the last few weeks, mainly from the north of England. Influenza virus B has been isolated whenever sought; virus A has not appeared. The first of these outbreaks was in West Wales at the end of September and beginning of October. Tyneside was affected early in October, and the disease has since spread slowly along the Tyne. Outbreaks have lately been reported from the Midlands, particularly Sheffield, Chesterfield, and Bradford, and most recently Hull. In the southern Midlands Gloucestershire has had several outbreaks, and at the end of last week Willesden in North-West London was affected, about two-thirds of the children in a school going down with the disease. Nearly everywhere it is schoolchildren who have fallen victims of the infection; adults have usually been spared. Attack rates in schools in affected areas have been about 60 to 70%. The disease is mild, generally lasting three to four days. The death rate for influenza has not shown any disproportionate increase over previous years, and Ministry of National Insurance first claims have not yet risen notably.

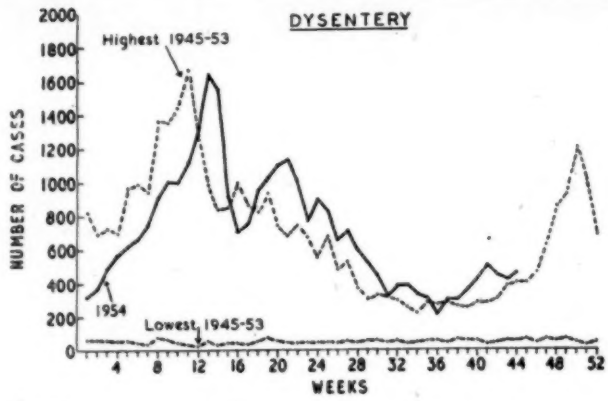
The investigation of influenza epidemics is discussed in the current *Monthly Bulletin of the Ministry of Health* (November, 1954), and details of the administrative arrangements recorded.

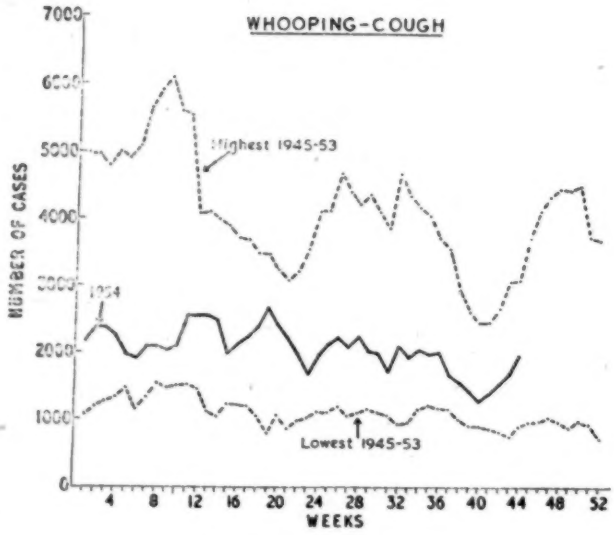
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1945–53 are shown thus - - - - - -, the figures for 1954 thus ————. Except for the curves showing notifications in 1954, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

The largest variations in the trends of the notifications of infectious diseases in England and Wales during the week ending November 6 were increases of 829 for measles, from 3,806 to 4,635, and 261 for whooping-cough, from 1,692 to 1,953, and a decrease of 58 for scarlet fever from 694 to 636.

The largest rises in the incidence of measles were 314 in Lancashire from 1,435 to 1,749, 98 in Nottinghamshire, from 132 to 230, 74 in Essex, from 157 to 231, and 63 in Denbighshire, from 47 to 110. In contrast to the rest of the country the incidence of measles declined slightly in the south, and the combined regions of the south-east and south-west counties had 50 fewer cases than in the preceding week. The largest rises in the incidence of whooping-cough were in the south-west—52 in Wiltshire, from 21 to 73, and 47 in Somersetshire, from 27 to 74—and the largest fall was 31 in Leicestershire, from 59 to 28. The only large variation in the trends of scarlet fever was a fall of 32 in Yorkshire West Riding, from 78 to 46. 14 cases of diphtheria were notified, being 6 more than in the preceding week.

59 cases of acute poliomyelitis were notified. These cases were 4 fewer for paralytic and 7 fewer for non-paralytic cases than in the preceding week. The largest returns were Lancashire 14 (Liverpool C.B. 2, Manchester C.B. 2, Ashton-in-Makerfield U.D. 2, Widnes M.B. 2), Yorkshire West Riding 9 (Sheffield C.B. 4, Doncaster C.B. 2, Leeds C.B. 2), Norfolk 5 (Wayland R.D. 4), and Derbyshire 4 (Chesterfield R.D. 3). In Scotland the peak incidence of poliomyelitis has occurred later than in England and Wales, and during the past 5 weeks the number of notifications has been at the highest level during the year. 26 cases were notified during the week; the largest returns were those of the cities of Glasgow 5, Aberdeen 3, and Inverness 3.

468 cases of dysentery were notified, being an increase of 44 on the total of the preceding week. The largest returns were Lancashire 152 (Morecambe and Heysham M.B. 37,

Oldham C.B. 26, Darwen M.B. 19, Liverpool C.B. 17), Yorkshire West Riding 74 (Huddersfield C.B. 23, Barnsley C.B. 14, Conisborough U.D. 11), London 38 (Chelsea 10, Islington 9), Lincolnshire 33 (Scunthorpe M.B. 30), Durham 31 (Jarrow M.B. 9), Middlesex 15, and Leicestershire 15 (Leicester C.B. 13). In Scotland the recent high level of incidence was maintained with 210 notifications, 6 more than in the preceding week. The largest centres of infection during the week were Glasgow 136, Edinburgh 19, and Dundee 16.

An outbreak of paratyphoid fever with 11 notifications has been reported from the city of Aberdeen.

Week Ending November 13

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 725, whooping-cough 1,939, diphtheria 17, measles 4,223, acute pneumonia 432, acute poliomyelitis 67, dysentery 575, paratyphoid fever 11, and typhoid fever 2.

Medical News

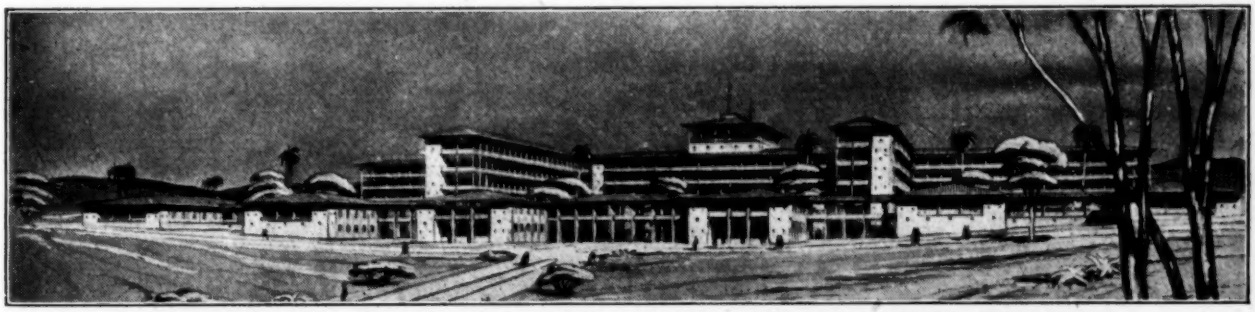
American Academy of General Practice.—The programme for the seventh annual assembly of the American Academy of General Practice is given in the October issue of the Academy's journal *G P*. It is interesting because it has been prepared in the light of replies to a questionary sent to every tenth member, and is thus claimed to be the kind of programme general practitioners feel would be most useful, "rather than what the committee felt they ought to have." There is a strong preference for panel discussions, and seven are included in the programme of the four-day meeting, on "Preserving the Doctor's Life and Usefulness," diabetes, "Childhood Disasters," peripheral vascular diseases, endocrinology, neurology, and "Handling the Athletic Injury." Most of the panel discussions last for one hour. Other major sessions are on allergy, and emergencies in infants and children. Among unusual subjects chosen for the shorter, half-hour sessions are "Breaking the Bad News," "Emotional Tragedies in Infancy and Childhood," and "Is it Hypospadias?" The programme organizer, Dr. ANDREW S. TOMB, remarks in his comments on the results of the questionary: "And, emphatically, it was stressed that the two prime requisites for any teacher are knowledge of the subject, and ability to present it understandably. Whether he was a 'big name' in the medical firmament was relatively unimportant." The assembly is being held in Los Angeles from March 28 to 31, 1955.

University College Hospital, Ibadan.—The picture at the foot of this page is an artist's drawing of the future University College Hospital at Ibadan, Nigeria, whose foundation stone was laid on November 18 by the Governor-General, Sir John Macpherson. It will be the first teaching hospital of its kind in British West Africa. The hospital will provide for the clinical training of the medical students from the University College at Ibadan. The College is closely linked with London University, and the premedical and preclinical courses there are recognized for the London M.B. But at present there is no hospital in West Africa where the student can complete the clinical part of his degree course, and as a result he is compelled to go abroad to finish his studies. It is hoped that the standard of teaching in the new hospital will be such as to lead to speedy recognition by London University. The hospital will consist of eight blocks of not less than five stories, with a total of nearly 500 beds. There will be a large out-patient department and adequate facilities for research. An output of 50 medical graduates a year is the aim. The cost, to be met by the Federal Government of Nigeria, is estimated at over £3½m. Ancillary buildings include a school of nursing and a nurses' home, a school of hygiene, and a medical students' hostel. The hospital is expected to open in October, 1956.

Fulbright Travel Grants.—Under the Fulbright Programme, competitive travel grants are offered to citizens of the United Kingdom and Colonies who wish to visit America for academic purposes. Candidates for the grants must hold a good university degree or a recognized professional qualification. For those intending to travel between June 1 and July 31, 1955, the closing date for applications is March 15; for those travelling after August 1, June 1. Details about the grants and application forms may be obtained from the United States Educational Commission in the United Kingdom, 55, Upper Brook Street, London, W.1. Candidates are advised to inform the Commission of their intention to apply for a grant as early as possible. The grants do not cover maintenance, tuition, or incidental expenses in the United States.

Union Internationale de la Presse Médicale.—At its conference in Turin last May (see *Journal*, July 31, p. 312) the Union Internationale de la Presse Médicale announced ten prizes of 50,000 lire each for original work published during the last few years in journals affiliated to the Union. The prizes were provided by the publishing house "Minerva Medica," the *Policlinico* group of journals, the scientific periodicals published by Cappelli of Bologna, *Riforma Medica*, and *Gazetta Medica Italiana*. Their award is now announced to the following: Dr. H. LABORIT (artificial hibernation), Dr. H. PEQUIGNOT (social medicine and medical legislation), Dr. J. NORDMANN (biochemistry of cirrhosis), Dr. A. CODOUNIS (hereditary methaemoglobinaemia), Dr. P. MIESCHER (pathogenesis of essential thrombocytopenia), Professor A. MORELLI (eosinophil leukaemia), Professor G. LENTI (A.C.T.H.), Professor G. VALLE (neonatal lung infections), Professor L. PROVENZALE (surgery of congenital heart disease), and Professor C. PAIS (megakaryocytes).

R.A.F. Medical and Dental Branches.—The 24th annual dinner was held at the Hyde Park Hotel on November 12. Among the guests were the Secretary of State for Air, the Chief of the Air Staff, Sir JOHN MCNEE, President of the B.M.A., and Sir WILFRID FISH, chairman of the Dental Board. The Director-General of the R.A.F. Medical Services, Air Marshal Sir JAMES KILPATRICK, in his address, referred to the dangerous experiment during the recent atomic test in Australia, carried out by a research team which included a medical pilot and a radiologist, both of whom received the Air Force Cross. He then went on to review the work of the Medical and Dental Branches during the current year. The Permanent Under-Secretary of State for Air replied to the toast of "The Guests," proposed by Wing-Commander G. H. DHENIN.



Reproduction of a drawing exhibited in 1953 in the architectural section of the Royal Academy.

Mr. L. R. Broster, surgeon at the Charing Cross Hospital, London, has been awarded the Bronze Medal of the Medical Association of South Africa in recognition of his "great services to this association and to the medical profession of South Africa in general." Special reference was made at the meeting of the federal council of the association to Mr. Broster's work on the committee of the Empire Medical Advisory Bureau, of which he has been chairman since 1950.

Dr. G. W. Ireland, of Pathhead, Midlothian, has succeeded Sir GEORGE LAIDLAW as chairman of the Scottish Council of Social Service. Dr. Ireland is a member of the Council of the B.M.A., and a member of the General Medical Council and of the Scottish Health Services Council.

Christmas Cards.—The National Association for Mental Health is offering three designs of Christmas card this year. A pamphlet illustrating them may be obtained from the headquarters of the association, 39, Queen Anne Street, London, W.1.

News in Brief.—The Telecobalt Unit at Bristol General Hospital was opened by Sir ERNEST ROCK CARLING on November 22.

Speaking at an antibiotics symposium sponsored by Lederle Laboratories in America, Dr. HENRY WELCH, director of antibiotics of the Food and Drugs Administration, said that the broad-spectrum antibiotics, chlortetracycline, oxytetracycline, tetracycline, and chloramphenicol, had accounted for $137m. out of the $262m. worth of antibiotics produced last year by United States manufacturers. An additional $19m. worth had gone for animal food supplements. Penicillin production had amounted to $58m., and streptomycin and dihydrostreptomycin to $35m. Since 1942, he added, upwards of 3,500 different antibiotic substances had been isolated and studied.

This year the Springarn Medal, which is awarded "for the highest achievement of an American negro," has been won by a distinguished Chicago dermatologist, Dr. T. K. LAWLESS. The medal is awarded by the National Association for the Advancement of Coloured People.

The proceedings of the symposium on oestrogen determination, described on p. 1157 of our November 13 issue, will be published in full in the *Memoirs of the Society for Endocrinology*. Copies will be available shortly (price 18s.) from the publishers, D. Dobson Ltd., 12, Park Place, St. James's, London, S.W.1.

COMING EVENTS

London Medical Orchestra.—Concert at the London Hospital, Whitechapel, E.1, December 13, 8.30 p.m. Works by Handel, Beethoven, and Schubert. Admission by programme (1s. 6d.).

Institute of Dermatology, London.—Exhibition on varicose conditions of the legs, December 6–24.

Exhibition of Kinematography, organized by the Kinematograph Group of the Royal Photographic Society, to illustrate "The Applications of Kinematography in Industry, Science, Medicine, Education, and other Specialized Fields," at 16, Princes Gate, London, S.W.7, December 3–18.

Bradshaw Lecture.—Professor LAMBERT ROGERS will lecture at the Royal College of Surgeons, Lincoln's Inn Fields, on "Tumours Involving the Spinal Cord and its Nerve Roots," December 8 at 4 p.m.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, November 29

CAMBRIDGE UNIVERSITY.—At Department of Pathology, Tennis Court Road, 5 p.m., Dr. J. Frimann-Dahl (Oslo): Radiological Examinations in Acute Abdominal Conditions.

●INSTITUTE OF NEUROLOGY.—5.30 p.m., Dr. Macdonald Critchley: Disturbances of Vision: At the Highest Level.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 4.30 p.m., Mr. R. A. Brews: Chorion Epithelioma and Vesicular Mole.

INSTITUTE OF PSYCHIATRY.—5.30 p.m., lecture-demonstration by Dr. E. Stengel.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. E. A. Carmichael: Some Observations on the Autonomic Nervous System.

Tuesday, November 30

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. L. Mary Pickford: Release and Action of Posterior Pituitary Hormones.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Mr. A. K. Monro: Varicose Conditions of the Leg.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Queen Charlotte's Maternity Hospital, 12 noon, Professor A. S. Duncan: Antepartum Haemorrhage.

ROYAL STATISTICAL SOCIETY: STUDY CIRCLE ON MEDICAL STATISTICS.—At Westminster Medical School, 6 p.m., Dr. L. Bernstein: Teaching of Medical Statistics.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., neurological demonstration by Dr. B. G. Parsons-Smith.

Wednesday, December 1

EDINBURGH CLINICAL CLUB.—4 p.m., visit to Astley-Ainslie Hospital.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Histopathology of Fungous Infection.

INSTITUTE OF LARYNGOLOGY.—5.30 p.m., Professor F. C. Ormerod: Otogenic Meningitis.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Dr. W. N. Mascall: Gonococcal Urethritis.

LIVERPOOL MEDICAL INSTITUTION.—(1) 4.30 p.m., Florence Blair-Bell Memorial Lecture by Sir Charles Dodds, F.R.S.: Thoughts on the Human Menaces—Infection and Cancer. (2) At Adelphi Hotel, Liverpool, 7.30 p.m., annual dinner.

MIDLAND MEDICAL SOCIETY.—At Birmingham Medical Institute, 154, Great Charles Street, 8.15 p.m., Sir Heneage Ogilvie: Common Mistakes in Surgical Diagnosis.

NOTTINGHAM MEDICO-CHIRURGICAL SOCIETY.—8.30 p.m., joint meeting with Nottingham Branch, B.M.A. Dr. G. E. Godber: Some Medical Problems within the National Health Service.

OXFORD UNIVERSITY MEDICAL SOCIETY.—At Taylorian Institution, 8.15 p.m., Professor H. A. Krebs, F.R.S.: Role of Biochemical Concepts in Medicine.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Professor J. N. Davidson: Recent Developments in the Biochemistry of the Nucleic Acids.

WORCESTER ROYAL INFIRMARY.—3.30 for 3.45 p.m., Dr. C. A. H. Watts: Depressive Disorders in General Practice.

Thursday, December 2

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. Rosalind Pitt-Rivers, F.R.S.: Thyroid Hormones.

FACULTY OF HOMOEOPATHY.—5 p.m., Dr. M. D. McCready: Wartime Homoeopathic Experiences in the Airborne Corps.

GLASGOW UNIVERSITY MEDICO-CHIRURGICAL SOCIETY.—At Glasgow University Union, 7.30 p.m., Dr. W. Ferguson Anderson: Rehabilitation of the Elderly Patient.

HONYMAN GILLESPIE LECTURE.—At University New Buildings, Edinburgh, 5 p.m., Dr. J. D. Matthews: Vascular Disease and Naturopathy in Diabetes Mellitus.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 4.30 p.m., Professor J. Young: Pelvic Osteo-Arthropathy of Pregnancy.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.30 p.m., otolaryngology lecture by Mr. D. H. Patey: Diseases of the Parotid Gland.

ST. ANDREWS UNIVERSITY.—At Physiology Department, Medical School, Small's Wynd, Dundee, 5 p.m., Professor B. G. Macgraith: Circulation in Acute Disease.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. D. J. Williams: neurology demonstration.

ST. JOHN'S HOSPITAL DERMATOLOGICAL SOCIETY.—4.30 p.m., clinical cases.

Friday, December 3

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. R. T Brain: Diseases of Children.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., clinical demonstration by Dr. N. C. Oswald and Mr. W. P. Cleland.

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL.—4.30 p.m., 7th Thomas Percy Legg Memorial Lecture by Mr. St. J. D. Buxton: The Simple Fracture.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—(1) 2 p.m., Mr. W. M. Capper: Side Effects of Gastric and Upper Intestinal Surgery. (2) 4 p.m., Dr. D. A. G. Galton: Chemotherapy of Leukaemia.

●ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., Professor C. F. W. Illingworth: Peptic Ulcer.

WHIPPS CROSS HOSPITAL MEDICAL SOCIETY.—8.30 p.m., Mr. D. Innes Williams: Intersex in Clinical Practice.

Saturday, December 4

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—10.30 a.m., symposium: Obstetrics and Gynaecology.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 11.15 a.m., Professor I. Donald: Neonatal Asphyxia.

KENT PAEDIATRIC AND CHILD HEALTH SOCIETY.—At Children's Clinic, Farnborough Hospital, Kent, 3 p.m., Symposium on Enuresis. Speakers, Dr. E. R. Bransby, Dr. A. Maberly, and Miss E. Shafto.

MIDLAND TUBERCULOSIS SOCIETY.—At Birmingham Chest Clinic, 3 p.m., Dr. N. C. Oswald: Chronic Bronchitis.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Daunt.—On October 10, 1954, at Kowloon Hospital, Hong Kong, to Bonnie, wife of Captain I. E. Daunt, R.A.M.C., a son—George Kieran Nicholas.

Jacoby.—On November 13, 1954, at Prospect Heights Hospital, Brooklyn, New York, U.S.A., to Thelma, wife of Dr. M. G. Jacoby, of Sunderland, England, a son—David Bernard.

DEATHS

Cameron.—On October 11, 1954, Malcolm Cameron, M.B., Surgeon Commander, R.N., retired, late of 15, Teesdale Road, Leytonstone, London, E.

Harper-Smith.—On November 4, 1954, at Green Meadow, Church Lane, Wivelsfield, Sussex, George Hastie Harper-Smith, M.D., aged 77.

Hayward.—On October 30, 1954, the result of an accident at Cambridge, Brian Harry Grant Hayward, M.B., B.S.

Any Questions ?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Varicosities of the Vulva in Pregnancy

Q.—*What treatment is advised for severe varicosities of the vulva and perineal region at the fifth month of pregnancy? They began at the second month, and were troublesome but not so severe in a previous pregnancy.*

A.—Varicose veins of the vulva and perineum occurring during pregnancy are usually treated conservatively by advising the patient to lie flat for half to one hour once or twice during the day, and to avoid standing so far as possible. Although they can cause much discomfort during mid-pregnancy they are often much less troublesome in the last three months, and nearly always disappear or become symptomless after delivery. They can, however, be treated by injections of sclerosing fluids such as quinine-urethrane, proprietary soap solutions, or sodium tetradecyl sulphate. Rather weaker solutions in smaller doses than those employed for varicose veins in non-pregnant women are advised, one or two sites being injected at each sitting. Extreme care over asepsis is necessary. But most authorities advise against injections for vulval varicose veins during pregnancy, their experience being that the procedure is technically difficult, that the results are not very satisfactory, and that there is some risk of producing local cellulitis and sloughing and spreading thrombosis to the deep veins of the pelvis and legs. Moreover, they argue that active treatment is not really necessary for a condition which is only troublesome for a strictly limited period of time. A few, however, are enthusiastic for it and claim good results. One of these is E. Solomons, who reports on 74 cases treated and describes the technique in detail.[1]

REFERENCE
[1] *Irish J. med. Sci.*, 1950, 353.

Involutional Melancholia in the Home

Q.—*What treatment is advised for a man of 62 with involutional melancholia who refuses E.C.T. or to visit a psychiatrist? What is the prognosis?*

A.—The answer to this question depends very largely on the type and severity of the disorder. Typically, one would be dealing with a man who for the first time in his life has developed an illness characterized by agitation, restlessness, depression, fear, and delusions of guilt, physical disease, or persecution. The illness may have come on suddenly and in response to a serious loss sustained by the patient (bereavement, loss of position, financial stress, surgical operations). On account of the great emotional distress, perplexity, and desire for punishment, the suicidal risk in such a case is considerable, and the patient's friends should be advised to arrange psychiatric treatment against the wish of the patient, whose unwillingness is often due to agitated indecision, profound hopelessness, and feelings of unworthiness. Especially when the onset has been acute and precipitated by an adequate external event, recovery is the usual outcome provided the patient can be guarded not only from suicide but also from secondary physical illnesses apt to occur in elderly people who are allowed to remain agitated and on a restricted diet, refusal of food being a very frequent symptom. There is a considerable weight of evidence to show that electro-convulsive treatment usually shortens this type of involutional depression, and that relapses will respond again.

If the relatives still refuse to arrange for psychiatric treatment after the above has been explained to them, the practitioner may under exceptionally favourable circumstances, so far as nursing and supervision are concerned, attempt treatment at home. This will be confined to ameliorating agitation and maintaining the physical, especially the nutritional, state. Heavy night sedation with paraldehyde (up to 3 fl. dr.—11 ml.) and barbitone (up to 15 gr.—1 g.) will be required. During the day frequent baths may help, rest in the open air, small doses of amylobarbitone sodium (1 to 3 gr.—65 to 200 mg.) or phenobarbitone (0.5 gr.—32 mg.) three times a day.

On the other hand, the label of "involutional melancholia" is often and justifiably attached to patients of lifelong neurotic disposition and poor adjustment to the emotional demands of life, who late in life develop relatively mild but persistent states characterized by anxiety, mild depression, and hypochondriacal preoccupations. In them the results with E.C.T. are often not very striking or lasting, and the family doctor can do more for patients of this type than the specialist. Mild and quick-acting hypnotics usually suffice at night. During the day various drugs containing amphetamine, phenobarbitone, belladonna in various combinations—for example, "drinamyl" or "bellergal," one tablet three times a day—should be tried out for their effect on restlessness and somatic sensations. Advice should be given on the daily routine with the object of providing the least possible scope for aimless agitation. It is mainly a question of encouraging the patient to carry on, as sooner or later much improvement can be expected, though many of the symptoms are likely to persist or to recur. There is little point in undertaking the care of a patient with mild involutional depression unless one is prepared to see him over many months and to maintain an optimistic front with fresh suggestions at every consultation in face of repetitive and rather aggravating complaints.

Artificial Ripening of Fruit

Q.—*Many fruits—home-grown as well as exotic—are picked off abnormally early and ripening is often speeded up later artificially. Could some information be given on the way the artificial ripening is brought about, and also whether fruits so processed differ from those left to mature on the tree, especially in vitamin content?*

A.—The primary difficulty is to define "ripe." If we take it to mean that stage at which a fruit has optimum flavour, bouquet, and texture, then most fruits are harvested unripe. Apples and pears ripen during marketing and storage; plums, peaches, and soft fruits do not travel well if fully ripe, and ripen after harvest; bananas must be harvested long before they are ripe to survive transport, and the same applies, for example, to tomatoes harvested in California for consumption in the eastern States of the U.S.A.

Most fruits can be ripened if held at a suitable temperature, say, not below 60° and not above 75° F. (15.6 and 23.9° C.), and the quality so obtained is good. The ripening of a few fruits—e.g., bananas and pears—can be accelerated by the addition of about one part of ethylene to each 1,000 parts of air in the ripening-room. I know of no work done to compare the composition of ethylene-ripened bananas with those ripened by heat alone, but they are not distinguishable by subjective tests. Some fruits are altered by ethylene, but are not ripened. Thus, plums develop odour more quickly but do not lose acid or gain in sweetness as compared with samples which have not been given ethylene. Some fruits do not respond to ethylene at all.

There are few data on change in vitamin content during ripening or storage. Tomatoes ripened off the plant are said to retain ascorbic acid well, and may show an increase as the red colour develops. Apples (not a very good source) may lose about 50% of vitamin C during five to six months of storage. Other vitamins—provitamin A, thiamin, riboflavine, niacin—are said to be well retained after harvest.

Sensitivity to Morphine

Q.—*An elderly doctor with coronary thrombosis has had numerous injections of morphine during the last sixteen years. He has experienced four unusual reactions shortly following an injection, as follows: (1) Six years ago after an injection in the left deltoid region his face and chest were immediately covered with a scarlatina-like rash which disappeared after a few minutes of itching. (2) Four months ago, after an injection in the left forearm, the same rash occurred immediately, with severe dyspnoea and headache. The rash was "burning" so keenly that he had to pull his clothes off. It was nearly half an hour before the symptoms wore off. (3) Three weeks ago, after an injection in the right calf, a rash appeared on the back which on cooling soon faded. (4) One week ago after an injection into the chest wall at 11 p.m. he was awakened many times in the night with cramp-like pains in his chest muscles, both back and front. What is the cause of these reactions, and why do they occur only occasionally? Should the morphine be replaced by some other drug, and, if so, which is recommended?*

A.—The cause of these reactions is a release of histamine. The patient has evidently become sensitive to morphine, and a person who is sensitive will suffer from reactions of this kind. It is difficult to say why they occur only occasionally, but it is true that they will become more frequent.

Amidone or phenadoxone might be tried. Both these drugs differ from morphine in structure, and therefore it is quite possible that the patient will not be sensitive to them. Alternatively, the reaction to the morphine could be prevented by taking an antihistamine tablet (mepyramine maleate or diphenhydramine hydrochloride) beforehand.

Tar Splashes

Q.—*In a variety of jobs in industry men occasionally receive splashes of either pitch or tar, and it is necessary for some simple and safe solvent to be available in first-aid rooms for their removal. What solvent do you recommend?*

A.—This is a very common injury in industry and many methods of treatment have been tried. The one preferred does not involve the use of a solvent but aims at removing the adhering patch by cetrimide. The splash and immediately surrounding skin are very gently rubbed with cotton-wool soaked in cetrimide, and after a few minutes the pitch comes away in one piece leaving either a blister or a raw area beneath. A blister should be emptied and covered by a sterile dressing. A raw area is better covered by a paraffin gauze dressing with a sterile dressing on top. Deep and extensive burns call for a skin graft.

This method of treatment has largely superseded treatment with solvents which leave a wide area of dirty skin behind—produced by the solution of the tar or pitch. If, however, such treatment is insisted upon toluene (toluol) will be found to be as effective and less painful than most other solvents.

Circumcision without Anaesthesia

Q.—*In "Pye's Surgical Handicraft" (16th ed., p. 359) a method of circumcising infants which is said to have long been in vogue in Australia is described. With no anaesthesia, the freed prepuce is crushed between bone forceps and then excised. There is no haemorrhage and sutures are not used. Up to what age may this operation be performed?*

A.—There is a great variety of opinion as to the age at which infants first feel and remember the pain of operations, but circumcision can certainly be performed without an anaesthetic during the first two or three weeks of life without obvious ill effects.

At the centres in which the bone forceps finds favour as an instrument of circumcision the method described is used in children of all ages, and in practised hands gives good results. The disadvantage of this eminently simple procedure is that there remains sufficient of the inner mucous membrane layer of the prepuce to cover the glans, and if contraction occurs at the site of the crushed ring of tissue the skin of the penis is drawn down from the shaft and reconstitutes the condition of phimosis. Many surgeons therefore trim away the excess mucosa after the initial cut with the bone forceps, and, so modified, the method is consistently satisfactory.

Toxic Effects of Vitamin A

Q.—*What are the features of overdosage with vitamin A? At what sort of dose do they appear? Have psychotic changes ever been recorded?*

A.—Acute poisoning with vitamin A has been reported in Arctic explorers who eat the liver of the polar bear; half a pound (227 g.) of this contains about 5 million I.U. of vitamin A. There is severe headache, nausea, and giddiness, marked drowsiness, and sometimes cramp. Acute poisoning may occur with doses over 1 million I.U.

Chronic poisoning has been reported mainly in infants and young children; it is unlikely to arise with doses below 100.000 I.U. daily, although a case has been reported of illness following 75,000 I.U. daily for six months. Dry irritable skin is invariable, and the hair is dry and sparse. The nails and teeth may break, and cortical hyperostoses of the ulna and metatarsals cause very tender swellings. The liver is often enlarged.

Irritability, mental sluggishness, and intense desire to sleep have been recorded, but not psychotic changes.

NOTES AND COMMENTS

Ringworm from Cattle.—Dr. A. MIDDLETON BROWN (Bristol) writes: Many years ago as a medical student I contracted an infection of my face by *Trichophyton megalosporon* from a puppy which had been reared at a farm where "Cattle Karry" was prevalent. The kerion lesion developed, and the application of a wide variety of fungicidal preparations was ineffective. The condition was cured by exposure to *x* rays together with manual depilation Care must be taken to regulate the dosage of *x* rays to prevent subsequent scarring. Your correspondent ("Any Questions?" November 6, p. 1120) should bear in mind the possibility of the infection being carried by dogs or cats to persons who have no direct contact with infected cattle.

OUR EXPERT writes: I quite agree with Dr. Middleton Brown that cattle ringworm may be spread by indirect contact, as I have had one man with this condition who has never been in contact with cattle, but whose son, living in the same house, was in charge of a pedigree herd. They used a common towel, and my patient developed ringworm on the beard area. I have no experience of cattle ringworm infection being carried by dogs or cats, though there is no reason why this should not be possible.

Correction.—We regret that in the leading article last week (p. 1213) entitled "Carcinogens in Cigarettes" Dr. R. E. Waller's name was wrongly printed as Walker.

Refresher Course Books.—Copies of the first two volumes of collected articles from the Refresher Course for General Practitioners published in the *Journal* are still available at 25s. (postage 1s.) each The first volume contains 55 articles and the second 60. Each article has been revised and brought up to date by its author.

Books of "Any Questions?"—The second and third books of "Any Questions?" are available at 7s. 6d. (postage 6d.) each. The third book contains a cumulative index to all the questions and answers in all three books.

These books may be obtained from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or through any bookseller.

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